STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 133526

TO: Ralph J Gitomer
Location: 3d65 / 3e71
Art Unit: 1651
Thursday, September 30, 2004

Case Serial Number: 10/000437

From: Noble Jarrell
Location: Biotech-Chem Library
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Noble.jarrell@uspto.gov

Search Notes

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=> d his

     (FILE 'HOME' ENTERED AT 09:57:54 ON 30 SEP 2004)

     FILE 'HCAPLUS' ENTERED AT 09:58:04 ON 30 SEP 2004
L1            1 US20020086342/PN

     FILE 'REGISTRY' ENTERED AT 09:58:22 ON 30 SEP 2004

     FILE 'HCAPLUS' ENTERED AT 09:58:26 ON 30 SEP 2004
L2              TRA L1 1- RN :       11 TERMS

     FILE 'REGISTRY' ENTERED AT 09:58:27 ON 30 SEP 2004
L3           11 SEA L2

     FILE 'WPIX' ENTERED AT 09:58:30 ON 30 SEP 2004
L4            1 US20020086342/PN

=> b hcap
FILE 'HCAPLUS' ENTERED AT 09:58:55 ON 30 SEP 2004
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FILE COVERS 1907 - 30 Sep 2004  VOL 141 ISS 14
FILE LAST UPDATED: 29 Sep 2004  (20040929/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


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L1   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2002:331864  HCAPLUS
DN   136:337033
ED   Entered STN:  03 May 2002
TI   Drug screening for inhibitors of mouse protein tyrosine phosphatase PTPbr7
     and their use in regulating nerve growth factor
IN   Schaeffer, Eric
PA   Pfizer Products Inc., USA
SO   Eur. Pat. Appl., 14 pp.
     CODEN: EPXXDW
DT   Patent
LA   English
IC   ICM  C12Q001-42
CC   7-1 (Enzymes)
     Section cross-reference(s): 1, 13
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     --------------      ----   --------    --------------------    --------
PI   EP 1201764          A2     20020502    EP 2001-124850          20011018
     EP 1201764          A3     20040107
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     US 2002086342       A1     20020704    US 2001-437             20011031 <--
     JP 2002355066       A2     20021210    JP 2001-334245          20011031
PRAI US 2000-244539P     P      20001031
CLASS
 PATENT NO.       CLASS  PATENT FAMILY CLASSIFICATION CODES
 --------------   -----  ----------------------------------------------
 EP 1201764       ICM    C12Q001-42
 EP 1201764       ECLA   C12Q001/42
AB   The present invention relates to novel assays for the identification of
     agents that inhibit the catalytic activity of mouse PTPbr7.  Substrates
```

for dephosphorylation include phosphorylated mitogen-activating kinase and small peptides contain phosphotyrosine residues. An assay for identifying inhibitors of PTPbr7 includes an assay buffer containing 50 mM TRIS, 0.15 M NaCl, 5 mM DTT, 0.1% BSA at pH 7.4 and a volume of 25.mu.L. The assay is terminated by adding malachite green dye, ammonium molybdate, and Tween-20 with incubation period of 15 min. Thereafter, the optical d. of free inorg. phosphate is spectrophotometrically measured at 620 nm and compared with a set of stds., containing varied amts. of inorg. phosphate. The invention also provides pharmaceutical compns. comprising such agents identified using the assays of the invention. The invention further provides methods of treatment comprising administering such pharmaceutical compns.

ST drug screening inhibitor PTPbr7; protein tyrosine phosphatase br7 human regulation nerve growth factor; fusion protein GST histidine tag PTPbr7

IT Signal transduction, biological
(PTPbr7 as neg. regulator of nerve growth factor; drug screening for inhibitors of human protein tyrosine phosphatase PTPbr7 and their use in regulating nerve growth factor)

IT Chimeric gene
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(PTPbr7 catalytic domain and GST encoded by; drug screening for inhibitors of human protein tyrosine phosphatase PTPbr7 and their use in regulating nerve growth factor)

IT Chimeric gene
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(PTPbr7 catalytic domain and histidine (6) tag encoded by; drug screening for inhibitors of human protein tyrosine phosphatase PTPbr7 and their use in regulating nerve growth factor)

IT Axon
(PTPbr7 inhibitor in stimulating growth of; drug screening for inhibitors of human protein tyrosine phosphatase PTPbr7 and their use in regulating nerve growth factor)

IT Brain
(PTPbr7 mRNA in; drug screening for inhibitors of human protein tyrosine phosphatase PTPbr7 and their use in regulating nerve growth factor)

IT Drug screening
Mus
(drug screening for inhibitors of human protein tyrosine phosphatase PTPbr7 and their use in regulating nerve growth factor)

IT Dephosphorylation, biological
(of phospho-MAPK or peptides containing phosphotyrosines by PTPbr7, inhibitors of; drug screening for inhibitors of human protein tyrosine phosphatase PTPbr7 and their use in regulating nerve growth factor)

IT Peptides, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphotyrosine, PTPbr7 in dephosphorylation of; drug screening for inhibitors of human protein tyrosine phosphatase PTPbr7 and their use in regulating nerve growth factor)

IT 9061-61-4, Nerve growth factor
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PTPbr7 as neg. regulator of; drug screening for inhibitors of human protein tyrosine phosphatase PTPbr7 and their use in regulating nerve growth factor)

IT 142243-02-5, Mitogen activated protein kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PTPbr7 in dephosphorylation of; drug screening for inhibitors of human protein tyrosine phosphatase PTPbr7 and their use in regulating nerve growth factor)

IT 373389-66-3, PTPBR7
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(PTPbr7, of mouse; drug screening for inhibitors of human protein tyrosine phosphatase PTPbr7 and their use in regulating nerve growth factor)

IT 148851-08-5 416848-49-2
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(amino acid sequence for PTPbr7 peptide substrate; drug screening for inhibitors of human protein tyrosine phosphatase PTPbr7 and their use in regulating nerve growth factor)

IT 13721-39-6, Sodium orthovanadate

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(as non-specific tyrosine phosphate inhibitor in drug screening assay; drug screening for inhibitors of human protein tyrosine phosphatase PTPbr7 and their use in regulating nerve growth factor)

IT 754-02-9
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(as substrate for PTPbr7 dephosphorylation in drug screening assay; drug screening for inhibitors of human protein tyrosine phosphatase PTPbr7 and their use in regulating nerve growth factor)

IT 50812-37-8D, Glutathione-S-transferase, PTPbr7 catalytic domain fusion product with
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(drug screening for inhibitors of human protein tyrosine phosphatase PTPbr7 and their use in regulating nerve growth factor)

IT 71-00-1D, L-Histidine, PTPbr7 catalytic domain fusion product with
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(tag; drug screening for inhibitors of human protein tyrosine phosphatase PTPbr7 and their use in regulating nerve growth factor)

IT 416933-31-8 416933-32-9
RL: PRP (Properties)
(unclaimed sequence; drug screening for inhibitors of mouse protein tyrosine phosphatase PTPbr7 and their use in regulating nerve growth factor)

=> b reg
FILE 'REGISTRY' ENTERED AT 09:59:01 ON 30 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 29 SEP 2004 HIGHEST RN 754169-63-6
DICTIONARY FILE UPDATES: 29 SEP 2004 HIGHEST RN 754169-63-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d ide l3 tot

L3 ANSWER 1 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN **416933-32-9** REGISTRY
CN DNA, d(G-A-C-A-C-T-C-T-G-G-T-A-A-A-T-C-T-T-C-G-G) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4: PN: EP1201764 PAGE: 11 unclaimed DNA
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PRP (Properties)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 2 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN

RN **416933-31-8** REGISTRY
CN DNA, d(C-T-T-A-G-C-C-T-A-G-A-G-T-G-G-G-G-T-T-G-G-C-G-G-C) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 3: PN: EP1201764 PAGE: 11 unclaimed DNA
FS NUCLEIC ACID SEQUENCE
MF Unspecified
CI MAN
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PRP (Properties)

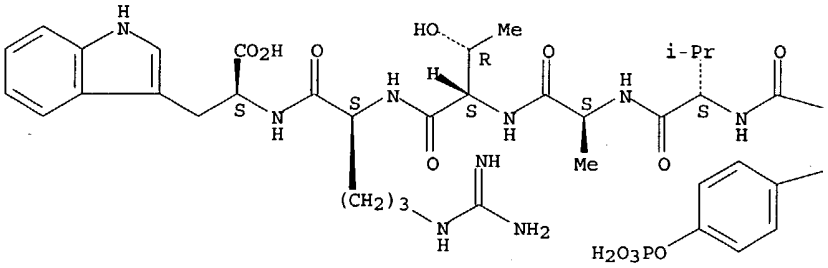
RELATED SEQUENCES AVAILABLE WITH SEQLINK

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 3 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN **416848-49-2** REGISTRY
CN L-Tryptophan, L-.alpha.-aspartyl-L-histidyl-L-threonylglycyl-L-phenylalanyl-L-leucyl-L-threonyl-L-.alpha.-glutamyl-O-phosphono-L-tyrosyl-L-valyl-L-alanyl-L-threonyl-L-arginyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2: PN: EP1201764 PAGE: 13 claimed sequence
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C78 H111 N20 O26 P
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)

Absolute stereochemistry.

PAGE 1-A



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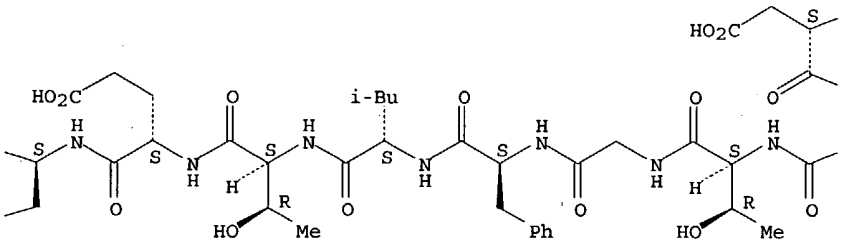

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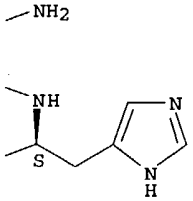


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 4 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN **373389-66-3** REGISTRY
CN Phosphatase, protein phosphotyrosine, SL (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Protein tyrosine phosphatase SL
CN Protein tyrosine phosphatase, receptor type Q
CN PTP-SL
CN PTPBR7
CN PTPRQ
MF Unspecified
CI MAN
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PROC (Process); PRP (Properties)

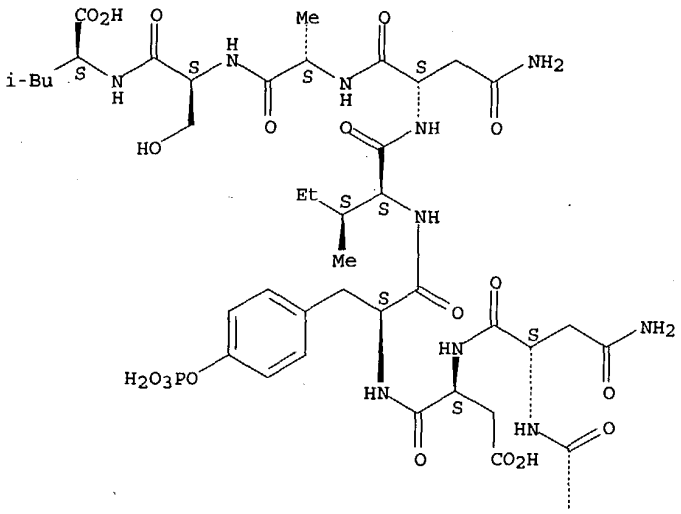
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
13 REFERENCES IN FILE CA (1907 TO DATE)
13 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 5 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN **148851-08-5** REGISTRY
CN L-Leucine, L-.alpha.-glutamyl-L-asparaginyl-L-.alpha.-aspartyl-O-phosphono-L-tyrosyl-L-isoleucyl-L-asparaginyl-L-alanyl-L-seryl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Leucine, N-[N-[N-[N2-[N-[N-[N-(N2-L-.alpha.-glutamyl-L-asparaginyl)-L-.alpha.-aspartyl]-O-phosphono-L-tyrosyl]-L-isoleucyl]-L-asparaginyl]-L-alanyl]-L-seryl]-
OTHER NAMES:
CN 1: PN: EP1201764 PAGE: 13 claimed protein
FS PROTEIN SEQUENCE; STEREOSEARCH
MF C44 H68 N11 O21 P
SR CA
LC STN Files: CA, CAPLUS, CHEMCATS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation)

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

PAGE 1-A



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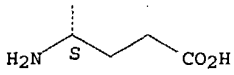

5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 6 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN **142243-02-5** REGISTRY
CN Kinase (phosphorylating), mitogen-activated protein (9CI) (CA INDEX NAME)
OTHER NAMES:
CN ERK
CN ERK kinase
CN Erk receptor tyrosine kinase
CN ERK/MAP kinase
CN Extracellular signal-regulated kinase
CN Extracellular signal-regulated protein kinase
CN Gene ERK protein kinase
CN MAP kinase
CN MAP/ERK kinase
CN MAPK
CN Mitogen-activated protein kinase
CN p43 MAP kinase
CN p43 Mitogen-activated protein kinase
CN p45 MAP kinase
DR 133876-94-5, 141349-99-7, 141350-00-7, 141616-09-3
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CEN, CIN, EMBASE, PROMT, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
9018 REFERENCES IN FILE CA (1907 TO DATE)
55 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
9063 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 7 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN **50812-37-8** REGISTRY
CN Transferase, glutathione S- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 173: PN: US20040058881 PAGE: 31 claimed sequence
CN 1: PN: US20040146861 FIGURE: 2 claimed sequence
CN 80: PN: WO2004025259 PAGE: 54 claimed sequence
CN 88: PN: WO2004025259 PAGE: 57 claimed sequence
CN Alkyltransferase, glutathione S-
CN Aralkyltransferase, glutathione S-
CN Aryltransferase, glutathione S-
CN Bromosulfophthalein glutathione transferase
CN E.C. 1.8.6.1
CN E.C. 2.5.1.12
CN E.C. 2.5.1.13
CN E.C. 2.5.1.14
CN E.C. 2.5.1.18
CN E.C. 4.4.1.7
CN Epoxidetransferase, glutathione S-
CN Fosfomycin:glutathione S-transferase
CN Glutathione S-alkyltransferase
CN Glutathione S-aralkyltransferase
CN Glutathione S-aralkyltransferase
CN Glutathione S-aryltransferase
CN Glutathione S-epoxidetransferase
CN Glutathione S-methyltransferase
CN Glutathione S-transferase
CN Glutathione S-transferase
CN Glutathione S-transferase .zeta.
CN Glutathione transferase
CN glutathione-S-transferase
CN Glutathionyl transferase
CN GSH S-aryltransferase
CN GSH transferase
CN Ligandins
CN Lyase, hydroxyalkylglutathione
CN Reductase, nitrate ester
CN S-(Hydroxyalkyl)glutathione lyase
CN Thiadiazolidine isomerase
DR 9029-41-8, 9052-42-0, 9079-09-8, 51570-22-0, 37277-81-9, 37290-93-0
MF Unspecified
CI MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CEN, CHEMCATS, CIN, CSCHEM, CSNB, EMBASE, MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PROMT, TOXCENTER, ULIDAT, USPAT2, USPATFULL
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Preprint; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
14626 REFERENCES IN FILE CA (1907 TO DATE)

781 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
14678 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 8 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN **13721-39-6** REGISTRY
CN Sodium vanadium oxide (Na3VO4) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Sodium vanadate(V) (Na3VO4) (6CI)
CN Vanadic acid (H3VO4), trisodium salt (8CI)
OTHER NAMES:
CN NSC 79534
CN Sodium o-vanadate
CN Sodium orthovanadate
CN Sodium orthovanadate (Na3VO4)
CN Sodium tetraoxovanadate(3-)
CN Sodium vanadate
CN Sodium vanadate (Na3VO4)
CN Trisodium orthovanadate
CN Trisodium vanadate
CN Vanadate (VO43-), trisodium, (T-4)-
DR 15066-70-3, 70904-59-5
MF Na . O . V
AF Na3 O4 V
CI COM, TIS
LC STN Files: AGRICOLA, AQUIRE, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, MSDS-OHS, NIOSHTIC, PIRA, PROMT, RTECS*, TOXCENTER, TULSA, ULIDAT, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PRP (Properties)

Component	Ratio	Component Registry Number
O	4	17778-80-2
V	1	7440-62-2
Na	3	7440-23-5

879 REFERENCES IN FILE CA (1907 TO DATE)
8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
883 REFERENCES IN FILE CAPLUS (1907 TO DATE)
21 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L3 ANSWER 9 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN **9061-61-4** REGISTRY
CN Nerve growth factor (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Nerve growth hormone
CN NGF
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration
LC STN Files: ADISINSIGHT, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, PHAR, PROMT, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Preprint; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)

RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
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RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

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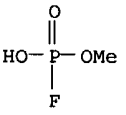
10172 REFERENCES IN FILE CA (1907 TO DATE)
137 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
10195 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 10 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN **754-02-9** REGISTRY
CN Phosphorofluoridic acid, monomethyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Methyl phosphorofluoridate ((MeO)(HO)FPO) (6CI, 7CI)
FS 3D CONCORD
MF C H4 F O3 P
CI COM
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: NORL (No role in record)



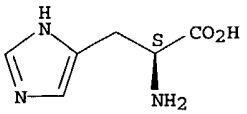
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L3 ANSWER 11 OF 11 REGISTRY COPYRIGHT 2004 ACS on STN
RN **71-00-1** REGISTRY
CN L-Histidine (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Histidine, L- (8CI)
OTHER NAMES:
CN (S)-.alpha.-Amino-1H-imidazole-4-propanoic acid
CN (S)-4-(2-Amino-2-carboxyethyl)imidazole
CN (S)-Histidine
CN 1H-Imidazole-4-alanine, (S)-
CN 1H-Imidazole-4-propanoic acid, .alpha.-amino-, (S)-
CN Glyoxaline-5-alanine
CN Histidine
CN L-(-)-Histidine
CN L-Alanine, 3-(1H-imidazol-4-yl)-
CN NSC 137773
FS STEREOSEARCH
DR 7006-35-1, 150-35-6, 54166-13-1, 155304-24-8, 35479-49-3, 35558-59-9, 45955-20-2
MF C6 H9 N3 O2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PROMT, PS, RTECS*, SPECINFO, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Preprint; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry. Rotation (-).



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34128 REFERENCES IN FILE CA (1907 TO DATE)
1379 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
34185 REFERENCES IN FILE CAPLUS (1907 TO DATE)
5 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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COPYRIGHT (C) 2004 THE THOMSON CORPORATION

FILE LAST UPDATED: 28 SEP 2004 <20040928/UP>
MOST RECENT DERWENT UPDATE: 200462 <200462/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
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>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE http://thomsonderwent.com/coverage/latestupdates/ <<<

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>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS: http://www.thomsonderwent.com/dwpifv <<<

>>> NEW DISPLAY FORMAT HITSTR ADDED ALLOWING DISPLAY OF HIT STRUCTURES WITHIN THE BIBLIOGRAPHIC DOCUMENT <<<

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L4 ANSWER 1 OF 1 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2002-418778 [45] WPIX
DNC C2002-118290
TI Identifying an agent that inhibits the catalytic activity of a tyrosine phosphatase, for treating neurodegenerative diseases, comprises quantitating dephosphorylation of a substrate by the enzyme, in the presence of the test agent.

DC B04 D16
IN SCHAEFFER, E
PA (PFIZ) PFIZER PROD INC; (SCHA-I) SCHAEFFER E
CYC 29
PI EP 1201764 A2 20020502 (200245)* EN 14 C12Q001-42
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
US 2002086342 A1 20020704 (200247) C12Q001-48 <--
CA 2360049 A1 20020430 (200248) EN C12Q001-42
JP 2002355066 A 20021210 (200311) 15 C12N015-09
ADT EP 1201764 A2 EP 2001-124850 20011018; US 2002086342 A1 Provisional US 2000-244539P 20001031, US 2001-437 20011031; CA 2360049 A1 CA 2001-2360049 20011029; JP 2002355066 A JP 2001-334245 20011031
PRAI US 2000-244539P 20001031; US 2001-437 20011031
IC ICM C12N015-09; C12Q001-42; C12Q001-48
ICS A61K038-43; A61K045-00; A61P025-00; A61P025-28; A61P043-00; C12Q001-00; C12Q001-02; C12Q001-44; G01N021-78; G01N033-15; G01N033-50; G01N033-573
AB EP 1201764 A UPAB: 20020717
NOVELTY - Identifying an agent that inhibits the catalytic activity of protein tyrosine phosphatase, PTPbr7, comprising quantitating and comparing the dephosphorylation in two cocktails, one containing PTPbr7, a substrate that can be dephosphorylated by PTPbr7 and a reducing buffer, and the other having the same ingredients but lacking the test agent.

DETAILED DESCRIPTION - Identifying an agent that inhibits the catalytic activity of protein tyrosine phosphatase, PTPbr7, comprising:

(a) combining, in a first cocktail, PTPbr7, a substrate capable of being dephosphorylated by PTPbr7, and a test agent, in an assay buffer containing a reducing buffer;

(b) preparing a second cocktail comprising all the ingredients of the first cocktail except for the text agent;

(c) incubating the first and second cocktails to allow dephosphorylation of the substrate by PTPbr7;

(d) quantitating the dephosphorylation in each of the cocktails; and

(e) comparing the amounts of dephosphorylation, where a PTPbr7 inhibitor is a test agent whose presence results in less dephosphorylation than it its absence.

INDEPENDENT CLAIMS are also included for the following:

(1) a pharmaceutical composition comprising an inhibitor of the catalytic activity of PTPbr7; and

(2) screening for an agent that inhibits the catalytic activity of PTPbr7, comprising:

(a) exposing cells or a cell line expressing PTPbr7 and capable of responding to nerve growth factor (NGF), to NGF, in the presence and absence of a test agent, to allow for a NGF response to occur in the presence of a PTPbr7 inhibitor;

(b) detecting the response; and

(c) comparing the response, where the PTPbr7 inhibitor is a test agent whose presence results in more of an NGF response than in its absence.

ACTIVITY - Nootropic; Neuroprotective. No suitable biological data is given.

MECHANISM OF ACTION - PTPbr7 inhibitor.

USE - The method is used to identify an agent that inhibits the catalytic activity of PTPbr7 (claimed). The agent can be used to treat neurodegenerative diseases.

Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-F01; B04-M01; B04-N08; B11-C07B2; B12-K04E; B14-J01A; D05-H09

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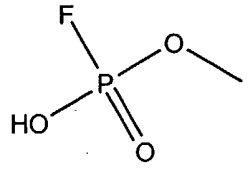

o-methylfluorophosphate

CH_4FO_3P

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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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provided by InfoChem.

STRUCTURE FILE UPDATES:   29 SEP 2004  HIGHEST RN 754169-63-6
DICTIONARY FILE UPDATES:  29 SEP 2004  HIGHEST RN 754169-63-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

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  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d ide l31 tot

L31  ANSWER 1 OF 24  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   333338-18-4  REGISTRY
CN   Phosphoric acid, mono(4-nitrophenyl) ester, disodium salt,
     hexahydrate (9CI)  (CA INDEX NAME)
MF   C6 H6 N O6 P . 6 H2 O . 2 Na
SR   CAS Client Services
LC   STN Files:   CHEMCATS
CRN  (330-13-2)
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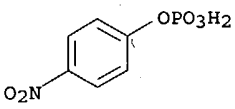

●2 Na

●6 H_2O

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L31  ANSWER 2 OF 24  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   208651-58-5  REGISTRY
CN   Phosphoric acid, mono(4-nitrophenyl) ester, monopotassium salt
     (9CI)  (CA INDEX NAME)
MF   C6 H6 N O6 P . K
SR   CAS Client Services
LC   STN Files:   CA, CAPLUS, CASREACT, CHEMCATS, CSCHEM
DT.CA  CAplus document type:  Journal
RL.NP  Roles from non-patents:  PREP (Preparation)
CRN  (330-13-2)
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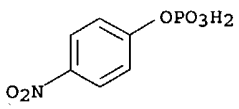
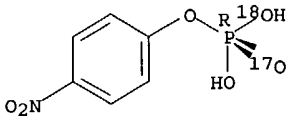


● K

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L31 ANSWER 3 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 112115-01-2 REGISTRY
CN **Phosphoric-17O-18O acid, 16O-(4-nitrophenyl) ester, disodium salt, (R)- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF **C6 H6 N O6 P . 2 Na**
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PREP (Preparation)
CRN (112114-76-8)

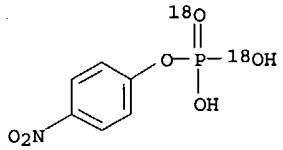
Absolute stereochemistry.



●2 Na

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

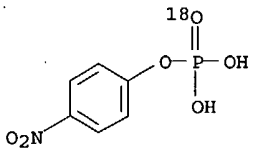
L31 ANSWER 4 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 112115-00-1 REGISTRY
CN **Phosphoric-18O2 acid, 16O-(4-nitrophenyl) ester, disodium salt (9CI)** (CA INDEX NAME)
MF **C6 H6 N O6 P . 2 Na**
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PREP (Preparation)



●2 Na

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L31 ANSWER 5 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 112114-99-5 REGISTRY
CN **Phosphoric-18O acid, 16O-(4-nitrophenyl) ester, disodium salt (9CI)** (CA INDEX NAME)
MF **C6 H6 N O6 P . 2 Na**
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PREP (Preparation)

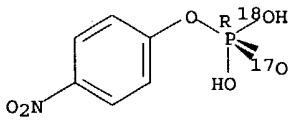


● 2 Na

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

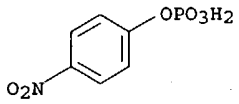
L31 ANSWER 6 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 112114-76-8 REGISTRY
CN **Phosphoric-17O-18O acid, 16O-(4-nitrophenyl) ester, (R)- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF **C6 H6 N O6 P**
CI COM
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L31 ANSWER 7 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 110347-83-6 REGISTRY
CN **Phosphoric acid, mono(4-nitrophenyl) ester, magnesium salt (1:1) (9CI)** (CA INDEX NAME)
MF **C6 H6 N O6 P . Mg**
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); RACT (Reactant or reagent)
CRN (330-13-2)



● Mg

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L31 ANSWER 8 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 88948-42-9 REGISTRY
CN **Phosphoric acid, mono(4-nitrophenyl) ester, calcium salt (9CI)** (CA INDEX NAME)
MF **C6 H6 N O6 P . x Ca**
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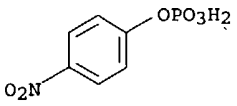
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: RACT (Reactant or reagent)

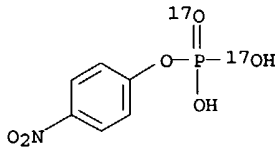
CRN (330-13-2)



●x Ca

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L31 ANSWER 9 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 87174-81-0 REGISTRY
CN **Phosphoric-17O2 acid, 16O-(4-nitrophenyl) ester, disodium salt (9CI)** (CA INDEX NAME)
MF **C6 H6 N O6 P . 2 Na**
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PRP (Properties)



●2 Na

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L31 ANSWER 10 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 81939-55-1 REGISTRY
CN **Phosphoric-17O-18O acid, 16O-(4-nitrophenyl) ester (9CI)** (CA INDEX NAME)
MF **C6 H6 N O6 P**
LC STN Files: CA, CAPLUS
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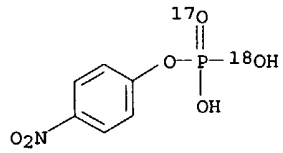
RL.NP Roles from non-patents: FORM (Formation, nonpreparative)



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L31 ANSWER 11 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 77849-47-9 REGISTRY
CN **Phosphoric acid, mono(4-nitrophenyl) ester, zirconium(4+) salt (2:1) (9CI)** (CA INDEX NAME)
MF **C6 H6 N O6 P . 1/2 Zr**
LC STN Files: CA, CAPLUS, USPATFULL
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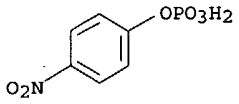
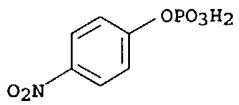
RL.P Roles from patents: PREP (Preparation)
CRN (330-13-2)



●1/2 Zr(IV)

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

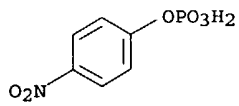
L31 ANSWER 12 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 76019-14-2 REGISTRY
CN **Phosphoric acid, mono(4-nitrophenyl) ester, magnesium salt (9CI)** (CA INDEX NAME)
MF **C6 H6 N O6 P . x Mg**
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study)
RL.NP Roles from non-patents: RACT (Reactant or reagent)
CRN (330-13-2)



●x Mg

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

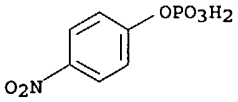
L31 ANSWER 13 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 75431-32-2 REGISTRY
CN **Phosphoric acid, mono(4-nitrophenyl) ester, thorium(4+) salt (2:1) (9CI)** (CA INDEX NAME)
MF **C6 H6 N O6 P . 1/2 Th**
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: PREP (Preparation)
RL.NP Roles from non-patents: PREP (Preparation)
CRN (330-13-2)



●1/2 Th(IV)

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L31 ANSWER 14 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 71735-29-0 REGISTRY
CN **Phosphoric acid, mono(4-nitrophenyl) ester, disodium salt, hydrate (9CI)** (CA INDEX NAME)
MF **C6 H6 N O6 P . x H2 O . 2 Na**
LC STN Files: BEILSTEIN*
(*File contains numerically searchable property data)
CRN (330-13-2)



● 2 Na

● x H_2O

L31 ANSWER 15 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 70951-20-1 REGISTRY
CN **Phosphoric acid, mono(4-nitrophenyl) ester, calcium salt (1:1) (9CI)** (CA INDEX NAME)
MF **C6 H6 N O6 P . Ca**
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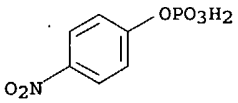
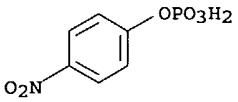
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: RACT (Reactant or reagent)
CRN (330-13-2)



● Ca

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L31 ANSWER 16 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 63035-79-0 REGISTRY
CN **Phosphoric acid, mono(4-nitrophenyl) ester, barium salt (1:1) (9CI)** (CA INDEX NAME)
MF **C6 H6 N O6 P . Ba**
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PREP (Preparation); NORL (No role in record)
CRN (330-13-2)

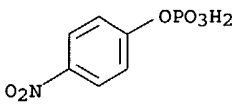


● Ba

12 REFERENCES IN FILE CA (1907 TO DATE)
12 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L31 ANSWER 17 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 54306-27-3 REGISTRY
CN **Phosphoric acid, mono(4-nitrophenyl) ester, sodium salt (9CI)** (CA INDEX NAME)
MF **C6 H6 N O6 P . x Na**
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMLIST
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

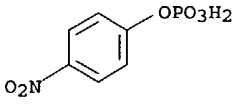
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation)
CRN (330-13-2)



●x Na

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

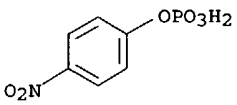
L31 ANSWER 18 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 51952-77-3 REGISTRY
CN **Phosphoric acid, mono(4-nitrophenyl) ester, disilver(1+) salt (9CI)** (CA INDEX NAME)
MF **C6 H6 N O6 P . 2 Ag**
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: RACT (Reactant or reagent)
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)
CRN (330-13-2)



●2 Ag(I)

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L31 ANSWER 19 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 32348-91-7 REGISTRY
CN **Phosphoric acid, mono(4-nitrophenyl) ester, diammonium salt (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN **Diammonium 4-nitrophenyl phosphate**
CN Diammonium p-nitrophenyl phosphate
MF **C6 H6 N O6 P . 2 H3 N**
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMLIST, IFICDB, IFIPAT, IFIUDB, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PROC (Process)
CRN (330-13-2)

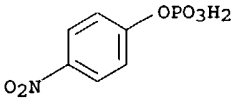


●2 NH_3

3 REFERENCES IN FILE CA (1907 TO DATE)

3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

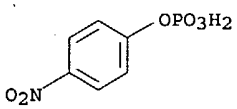
L31 ANSWER 20 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 32348-90-6 REGISTRY
CN **Phosphoric acid, mono(4-nitrophenyl) ester, magnesium salt (1:2) (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN Dimagnesium p-nitrophenyl phosphate
MF **C6 H6 N O6 P . 2 Mg**
LC STN Files: CA, CAPLUS, CHEMCATS, CHEMLIST, IFICDB, IFIPAT, IFIUDB, USPATFULL
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PROC (Process)
CRN (330-13-2)



●2 Mg

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

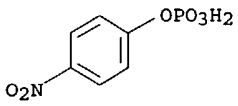
L31 ANSWER 21 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 16785-19-6 REGISTRY
CN **Phosphoric acid, mono(4-nitrophenyl) ester, dipotassium salt (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phosphoric acid, mono(p-nitrophenyl) ester, dipotassium salt (8CI)
MF **C6 H6 N O6 P . 2 K**
CRN (330-13-2)



●2 K

L31 ANSWER 22 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 4264-83-9 REGISTRY
CN **Phosphoric acid, mono(4-nitrophenyl) ester, disodium salt (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phenol, p-nitro-, di-H phosphate, disodium salt (7CI)
CN Phenol, p-nitro-, phosphate disodium salt (6CI)
CN Phosphoric acid, mono(p-nitrophenyl) ester, disodium salt (8CI)
OTHER NAMES:
CN **4-Nitrophenyl phosphate disodium salt**
CN **Disodium 4-nitrophenyl phosphate**
CN **Disodium mono(4-nitrophenyl) phosphate**
CN Disodium p-nitrophenyl phosphate
CN p-Nitrophenyl disodium phosphate
CN p-Nitrophenyl phosphate disodium salt
CN **p-Nitrophenylphosphate sodium salt**
CN p-NPP disodium salt
MF **C6 H6 N O6 P . 2 Na**
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, IFICDB, IFIPAT, IFIUDB, MSDS-OHS, TOXCENTER, USPATFULL

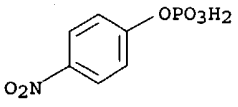
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
CRN (330-13-2)



●2 Na

80 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
80 REFERENCES IN FILE CAPLUS (1907 TO DATE)
6 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L31 ANSWER 23 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 4154-43-2 REGISTRY
CN **Phosphoric acid, mono(4-nitrophenyl) ester, monosodium salt (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phenol, p-nitro-, di-H phosphate, sodium salt (7CI)
CN Phosphoric acid, mono(p-nitrophenyl) ester, monosodium salt (8CI)
OTHER NAMES:
CN Sodium p-nitrophenyl phosphate
MF **C6 H6 N O6 P . Na**
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CSCHEM, TOXCENTER
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); NORL (No role in record)
CRN (330-13-2)

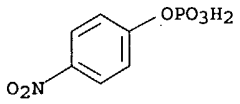


● Na

22 REFERENCES IN FILE CA (1907 TO DATE)
22 REFERENCES IN FILE CAPLUS (1907 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L31 ANSWER 24 OF 24 REGISTRY COPYRIGHT 2004 ACS on STN
RN 330-13-2 REGISTRY
CN **Phosphoric acid, mono(4-nitrophenyl) ester (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phenol, p-nitro-, dihydrogen phosphate (6CI)
CN Phosphoric acid, mono(p-nitrophenyl) ester (8CI)
CN Phosphoric acid, p-nitrophenyl ester (6CI)

OTHER NAMES:
CN **4-Nitrophenyl dihydrogen phosphate**
CN **4-Nitrophenyl phosphate**
CN NPP
CN NSC 404086
CN p-Nitrophenol phosphate
CN p-Nitrophenyl dihydrogen phosphate
CN p-Nitrophenyl phosphate
CN PNPP
FS 3D CONCORD
MF **C6 H6 N O6 P**
CI COM
LC STN Files: AGRICOLA; BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, EMBASE, GMELIN*, IFICDB, IFIPAT, IFIUDB, MEDLINE, MSDS-OHS, NIOSHTIC, PROMT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1609 REFERENCES IN FILE CA (1907 TO DATE)
24 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1609 REFERENCES IN FILE CAPLUS (1907 TO DATE)
31 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> => d his

(FILE 'HOME' ENTERED AT 09:57:54 ON 30 SEP 2004)

FILE 'HCAPLUS' ENTERED AT 09:58:04 ON 30 SEP 2004
L1 1 US20020086342/PN

FILE 'REGISTRY' ENTERED AT 09:58:22 ON 30 SEP 2004

FILE 'HCAPLUS' ENTERED AT 09:58:26 ON 30 SEP 2004
L2 TRA L1 1- RN : 11 TERMS

FILE 'REGISTRY' ENTERED AT 09:58:27 ON 30 SEP 2004
L3 11 SEA L2

FILE 'WPIX' ENTERED AT 09:58:30 ON 30 SEP 2004
L4 1 US20020086342/PN

FILE 'REGISTRY' ENTERED AT 10:15:37 ON 30 SEP 2004
E PTPBR7/CN
L5 1 L3 AND PTPBR7
L6 4 PTPBR7

FILE 'HCAPLUS' ENTERED AT 10:18:12 ON 30 SEP 2004
L7 13 L5
L8 5952 (PHOSPHATASE (2A) PROTEIN (2A) (PHOSPHOTYROSINE OR TYROSINE) OR

```
                E DESPHOSPHORYLATION, BIOLOGICAL/CT
                E DEPHOSPHORYLATION, BIOLOGICAL/CT
                E DEPHOSPHORYLATION/CT
                E E3+ALL
                E E2+ALL
L9          5081 "DEPHOSPHORYLATION, BIOLOGICAL"/CT
                E DRUG SCREENING/CT
                E E3+ALL
                E CHEMICAL LIBRARY/CT
                E E3+ALL
                E E5+ALL
                E DRUG DISCOVERY/CT
                E E3+ALL
L10        39357 DRUG DISCOVERY+NT/CT
L11           12 L7-8 AND L9 AND L10
                E SCHAEFFER E/AU
L12           48 E3,E16
L13        10984 PFIZER/CS,PA
L14            1 L11 AND L12
L15            1 L11 AND L13
L16            1 L14-15
L17           11 L11 NOT L16
L18            8 L17 AND (PY<=2000 OR AY<=2000 OR PRY<=2000 OR PD<20001031 OR AD

     FILE 'REGISTRY' ENTERED AT 10:42:04 ON 30 SEP 2004
                E MAPK-P/CN
                E P-NITROPHENYLPHOSPHATE/CN
L19            1 E4

     FILE 'HCAPLUS' ENTERED AT 10:44:39 ON 30 SEP 2004
                E IMMUNOASSAY/CT
                E E3+ALL
L20        51907 IMMUNOASSAY+OLD,NT/CT
                E IMMUNOCHEMICAL ANALYSIS/CT
                E E3+ALL
L21         3702 IMMUNOCHEMICAL ANALYSIS/CT (L) IMMUNOASSAY?
L22            3 L7-8 AND L9 AND L20-21
L23            0 L22 AND L12-13
L24            2 L22 AND (PY<=2000 OR AY<=2000 OR PRY<=2000 OR PD<20001031 OR AD
L25           10 L24 OR L18

     FILE 'REGISTRY' ENTERED AT 10:48:06 ON 30 SEP 2004
                E O-METHYLFLUOROPHOSPHATE/CN
L26            0 CH4FO3P
L27           85 C6H6NO6P AND C6/ES
L28           33 L27 NOT ((PMS OR MAN OR IDS)/CI OR COMPD OR COMPOUND OR UNSPECI
L29           25 L28 AND 4(1A) NITROPHENYL
L30           24 L29 NOT PHOSPHONIC (1A) ACID
L31           24 L19 OR L30

     FILE 'HCAPLUS' ENTERED AT 10:57:29 ON 30 SEP 2004
L32         1715 L31
L33         4950 (PHOSPHORIC (1A) ACID (1A) MONO (1A) 4 (1A) NITROPHENYL (1A) ES
                E PHOSPOPROTEIN/CT
                E PHOSPHOPROTEIN/CT
                E PHOSPHOPROTEINS/CT
                E E3+ALL
L34       123837 PHOSPHOPROTEINS+NT/CT
L35            3 L25 AND L32-34
                E HIGH THROUGHPUT SCREENING/CT
                E E3+ALL
L36         3930 HIGH THROUGHPUT SCREENING/CT
L37           19 L36 AND L7-8
L38            1 L37 AND L9
L39            0 L38 AND L12-13
L40            0 L38 AND (PY<=2000 OR AY<=2000 OR PRY<=2000 OR PD<20001031 OR AD

     FILE 'EMBASE' ENTERED AT 11:27:02 ON 30 SEP 2004
L41         5352 L7-8
L42        73832 (E5.160.160.680. OR G1.550.100.690. OR H1.150.150.680.)/CT
L43       425108 (E1.50.150.225. OR E5.680.202. OR E1.800. OR E5.795.)/CT
L44           40 L41 AND L42 AND L43
                E SCHAEFFER E/AU
L45           54 E3
L46         4201 PFIZER/CS
L47            0 L44 AND L45-46
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L48          17 L44 AND PY<=2001
L49       45600 D4.680.695./CT
L50           3 L48 AND (L31 OR L33 OR L49)
                SEL AN 2-4 6 9-14 L48
                SEL AN 1 3 L50
L51          11 E1-12 AND (L48 OR L50)

     FILE 'WPIX' ENTERED AT 12:49:49 ON 30 SEP 2004
L52         379 L8
L53       99105 (B11-C08? OR C11-C08? OR B11-C10? OR C11-C10?)/MC OR G01N033-53
L54         958 DEPHOSPHORYLAT?/BIX
L55          12 L52 AND L53 AND L54
                E SCHAEFFER E/AU
L56          10 E3
L57        4980 PFIZER/CS,PA
L58           0 L55 AND L56-57
L59           4 L55 NOT (PY>2001 OR PRY>2001 OR AY>2001)
                SEL AN 1-3
L60           3 E1-3 AND L59

=> b hcap
FILE 'HCAPLUS' ENTERED AT 13:00:55 ON 30 SEP 2004
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FILE COVERS 1907 - 30 Sep 2004  VOL 141 ISS 14
FILE LAST UPDATED: 29 Sep 2004  (20040929/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> d all l16 tot

L16  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2002:331864  HCAPLUS
DN   136:337033
ED   Entered STN:  03 May 2002
TI   Drug screening for inhibitors of mouse protein tyrosine
     phosphatase PTPbr7 and their use in regulating nerve
     growth factor
IN   Schaeffer, Eric
PA   Pfizer Products Inc., USA
SO   Eur. Pat. Appl., 14 pp.
     CODEN: EPXXDW
DT   Patent
LA   English
IC   ICM  C12Q001-42
CC   7-1 (Enzymes)
     Section cross-reference(s): 1, 13
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     ---------------     ----   --------    --------------------    --------
PI   EP 1201764           A2    20020502    EP 2001-124850          20011018
     EP 1201764           A3    20040107
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     US 2002086342        A1    20020704    US 2001-437             20011031
     JP 2002355066        A2    20021210    JP 2001-334245          20011031
PRAI US 2000-244539P      P     20001031
CLASS
 PATENT NO.      CLASS  PATENT FAMILY CLASSIFICATION CODES
 --------------  -----  ----------------------------------------------
 EP 1201764      ICM    C12Q001-42
```

EP 1201764 ECLA C12Q001/42

AB The present invention relates to novel assays for the identification of agents that inhibit the catalytic activity of mouse **PTPbr7.** Substrates for dephosphorylation include phosphorylated mitogen-activating kinase and small peptides contain phosphotyrosine residues. An assay for identifying inhibitors of **PTPbr7** includes an assay buffer containing 50 mM TRIS, 0.15 M NaCl, 5 mM DTT, 0.1% BSA at pH 7.4 and a volume of 25.mu.L. The assay is terminated by adding malachite green dye, ammonium molybdate, and Tween-20 with incubation period of 15 min. Thereafter, the optical d. of free inorg. phosphate is spectrophotometrically measured at 620 nm and compared with a set of stds., containing varied amts. of inorg. phosphate. The invention also provides pharmaceutical compns. comprising such agents identified using the assays of the invention. The invention further provides methods of treatment comprising administering such pharmaceutical compns.

ST drug screening inhibitor **PTPbr7**; **protein tyrosine phosphatase** br7 human regulation nerve growth factor; fusion protein GST histidine tag **PTPbr7**

IT Signal transduction, biological
(**PTPbr7** as neg. regulator of nerve growth factor; drug screening for inhibitors of human **protein tyrosine phosphatase PTPbr7** and their use in regulating nerve growth factor)

IT Chimeric gene
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**PTPbr7** catalytic domain and GST encoded by; drug screening for inhibitors of human **protein tyrosine phosphatase PTPbr7** and their use in regulating nerve growth factor)

IT Chimeric gene
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**PTPbr7** catalytic domain and histidine (6) tag encoded by; drug screening for inhibitors of human **protein tyrosine phosphatase PTPbr7** and their use in regulating nerve growth factor)

IT Axon
(**PTPbr7** inhibitor in stimulating growth of; drug screening for inhibitors of human **protein tyrosine phosphatase PTPbr7** and their use in regulating nerve growth factor)

IT Brain
(**PTPbr7** mRNA in; drug screening for inhibitors of human **protein tyrosine phosphatase PTPbr7** and their use in regulating nerve growth factor)

IT **Drug screening**
Mus
(drug screening for inhibitors of human **protein tyrosine phosphatase PTPbr7** and their use in regulating nerve growth factor)

IT **Dephosphorylation, biological**
(of phospho-MAPK or peptides containing phosphotyrosines by **PTPbr7**, inhibitors of; drug screening for inhibitors of human **protein tyrosine phosphatase PTPbr7** and their use in regulating nerve growth factor)

IT Peptides, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphotyrosine, **PTPbr7** in dephosphorylation of; drug screening for inhibitors of human **protein tyrosine phosphatase PTPbr7** and their use in regulating nerve growth factor)

IT 9061-61-4, Nerve growth factor
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**PTPbr7** as neg. regulator of; drug screening for inhibitors of human **protein tyrosine phosphatase PTPbr7** and their use in regulating nerve growth factor)

IT 142243-02-5, Mitogen activated protein kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**PTPbr7** in dephosphorylation of; drug screening for inhibitors of human **protein tyrosine phosphatase PTPbr7** and their use in regulating nerve growth factor)

IT **373389-66-3, PTPBR7**

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(**PTPbr7**, of mouse; drug screening for inhibitors of human **protein tyrosine phosphatase PTPbr7** and their use in regulating nerve growth factor)

IT 148851-08-5 416848-49-2
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(amino acid sequence for **PTPbr7** peptide substrate; drug screening for inhibitors of human **protein tyrosine phosphatase PTPbr7** and their use in regulating nerve growth factor)

IT 13721-39-6, Sodium orthovanadate
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(as non-specific tyrosine phosphate inhibitor in drug screening assay; drug screening for inhibitors of human **protein tyrosine phosphatase PTPbr7** and their use in regulating nerve growth factor)

IT 754-02-9
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(as substrate for **PTPbr7** dephosphorylation in drug screening assay; drug screening for inhibitors of human **protein tyrosine phosphatase PTPbr7** and their use in regulating nerve growth factor)

IT 50812-37-8D, Glutathione-S-transferase, **PTPbr7** catalytic domain fusion product with
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(drug screening for inhibitors of human **protein tyrosine phosphatase PTPbr7** and their use in regulating nerve growth factor)

IT 71-00-1D, L-Histidine, **PTPbr7** catalytic domain fusion product with
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(tag; drug screening for inhibitors of human **protein tyrosine phosphatase PTPbr7** and their use in regulating nerve growth factor)

IT 416933-31-8 416933-32-9
RL: PRP (Properties)
(unclaimed sequence; drug screening for inhibitors of mouse **protein tyrosine phosphatase PTPbr7** and their use in regulating nerve growth factor)

=> d all l25 tot

L25 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:376284 HCAPLUS
DN 138:363219
ED Entered STN: 16 May 2003
TI Methods for the screening of agents modulating **protein tyrosine phosphatase** L1 (PTPL1) binding to the NMDA receptor or PTPL1-mediated dephosphorylation of NMDA receptor for the treatment of human diseases
IN Jerecic, Jasna; Braithwaite, Steven; Kask, Kalev; Liu, Jenkuei; Melcher, Thorsten
PA USA
SO U.S. Pat. Appl. Publ., 16 pp., Cont.-in-part of U.S. Ser. No. 774,481.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-00
ICS C12Q001-68; G01N033-53; G01N033-567
NCL 435007200; 435006000; 514001000
CC 2-8 (Mammalian Hormones)
Section cross-reference(s): 63
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003092071	A1	20030515	US 2002-246837	20020918 <--
	US 2001049348	A1	20011206	US 2001-774481	20010130 <--
	US 6521414	B2	20030218		
	US 2004072275	A1	20040415	US 2003-633109	20030801 <--

PRAI US 2000-179453P P 20000201 <--
US 2001-774481 A2 20010130
US 2002-246837 A2 20020918

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2003092071	ICM	A61K031-00
	ICS	C12Q001-68; G01N033-53; G01N033-567
	NCL	435007200; 435006000; 514001000
US 2004072275	ECLA	C12Q001/42; G01N033/94B <--

AB The present invention relates to the identification of a binding between NMDA receptor (NMDA-R) subunits and a **protein tyrosine phosphatase** (PTP), e.g., PTPL1. The present invention provides methods for screening a PTP agonist or antagonist that modulates NMDA-R signaling. The present invention also provides methods and compns. for treatment of disorders mediated by abnormal NMDA-R signaling. The present invention further provides methods for isolating PTPL1 from a biol. preparation

ST NMDA receptor **protein tyrosine phosphatase**
PTPL1 screening treatment

IT Nervous system, disease
(Huntington's chorea; methods for the screening of agents modulating **protein tyrosine phosphatase** L1 (PTPL1) binding to the NMDA receptor or PTPL1-mediated dephosphorylation of NMDA receptor for the treatment of human diseases)

IT Glutamate receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NMDA-binding; methods for the screening of agents modulating **protein tyrosine phosphatase** L1 (PTPL1) binding to the NMDA receptor or PTPL1-mediated dephosphorylation of NMDA receptor for the treatment of human diseases)

IT Drug tolerance
(alc.; methods for the screening of agents modulating **protein tyrosine phosphatase** L1 (PTPL1) binding to the NMDA receptor or PTPL1-mediated dephosphorylation of NMDA receptor for the treatment of human diseases)

IT Pain
(chronic; methods for the screening of agents modulating **protein tyrosine phosphatase** L1 (PTPL1) binding to the NMDA receptor or PTPL1-mediated dephosphorylation of NMDA receptor for the treatment of human diseases)

IT Mental disorder
(dementia; methods for the screening of agents modulating **protein tyrosine phosphatase** L1 (PTPL1) binding to the NMDA receptor or PTPL1-mediated dephosphorylation of NMDA receptor for the treatment of human diseases)

IT Brain, disease
(injury; methods for the screening of agents modulating **protein tyrosine phosphatase** L1 (PTPL1) binding to the NMDA receptor or PTPL1-mediated dephosphorylation of NMDA receptor for the treatment of human diseases)

IT Alzheimer's disease
Analgesics
Anti-Alzheimer's agents
Anticonvulsants
Antipsychotics
Dephosphorylation, biological
Drug dependence
Drug screening
Epilepsy
Human
Molecular association
Nervous system agents
Schizophrenia
(methods for the screening of agents modulating **protein tyrosine phosphatase** L1 (PTPL1) binding to the NMDA receptor or PTPL1-mediated dephosphorylation of NMDA receptor for the treatment of human diseases)

IT Nerve, disease
(motor; methods for the screening of agents modulating **protein tyrosine phosphatase** L1 (PTPL1) binding to the NMDA receptor or PTPL1-mediated dephosphorylation of NMDA receptor for the treatment of human diseases)

IT Nerve, disease
(neuropathy; methods for the screening of agents modulating **protein tyrosine phosphatase** L1 (PTPL1) binding to the NMDA receptor or PTPL1-mediated dephosphorylation of

NMDA receptor for the treatment of human diseases)
IT Signal transduction, biological
(of activated NMDA receptor; methods for screening of agents modulating **protein tyrosine phosphatase** L1 (PTPL1) binding to the NMDA receptor or PTPL1-mediated dephosphorylation of NMDA receptor for treatment of human diseases)
IT Mental disorder
(psychosis; methods for the screening of agents modulating **protein tyrosine phosphatase** L1 (PTPL1) binding to the NMDA receptor or PTPL1-mediated dephosphorylation of NMDA receptor for the treatment of human diseases)
IT Nervous system, disease
(spinocerebellar degeneration; methods for the screening of agents modulating **protein tyrosine phosphatase** L1 (PTPL1) binding to the NMDA receptor or PTPL1-mediated dephosphorylation of NMDA receptor for the treatment of human diseases)
IT Brain, disease
(stroke; methods for the screening of agents modulating **protein tyrosine phosphatase** L1 (PTPL1) binding to the NMDA receptor or PTPL1-mediated dephosphorylation of NMDA receptor for the treatment of human diseases)
IT Head, disease
(trauma; methods for the screening of agents modulating **protein tyrosine phosphatase** L1 (PTPL1) binding to the NMDA receptor or PTPL1-mediated dephosphorylation of NMDA receptor for the treatment of human diseases)
IT 300851-68-7, PTP-L1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(agonists and antagonists; methods for the screening of agents modulating **protein tyrosine phosphatase** L1 (PTPL1) binding to the NMDA receptor or PTPL1-mediated dephosphorylation of NMDA receptor for the treatment of human diseases)

L25 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:575291 HCAPLUS
DN 137:137209
ED Entered STN: 02 Aug 2002
TI Three dimensional format biochips
IN Fagnani, Roberto; Hahn, Sonnkap; Dong, Xiaofan; Pircher, Tony; Matsumoto, Sandra; Tsinberg, Pavel
PA Biocept, Inc., USA
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12Q001-68
CC 9-1 (Biochemical Methods)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002059372	A2	20020801	WO 2001-US51265	20011026 <--
	WO 2002059372	A3	20020919		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1328810	A2	20030723	EP 2001-994529	20011026 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004518138	T2	20040617	JP 2002-559854	20011026 <--
PRAI	US 2000-243699P	P	20001026	<--	
	WO 2001-US51265	W	20011026		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002059372	ICM	C12Q001-68
JP 2004518138	FTERM	4B024/AA11; 4B024/AA19; 4B024/AA20; 4B024/CA01; 4B024/CA11; 4B024/HA11; 4B024/HA20; 4B029/AA07; 4B029/AA21; 4B029/BB15; 4B029/BB20; 4B029/CC01; 4B029/CC02; 4B029/CC05; 4B029/FA12; 4B029/FA15;

4B063/QA01; 4B063/QA05; 4B063/QQ42; 4B063/QQ49;
4B063/QQ52; 4B063/QQ79; 4B063/QR32; 4B063/QR35;
4B063/QR38; 4B063/QR48; 4B063/QR56; 4B063/QR82;
4B063/QS32; 4B063/QS36; 4B063/QX02 <--

AB A biochip is formed with a plurality of optically clear hydrogel cells attached to the top surface of a solid substrate in the form of an array. Each of the cells is formed of a hydrogel of polyethylene glycol, polypropylene glycol or a copolymer thereof having reactive isocyanate groups. Nonhybridization binding entities are immobilized in these cells, which entities are effective to selectively sequester a target protein or other comparable biomol. Different binding entities are immobilized in different cells to create a biochip that can be used to assay for a number of target biomols.

ST biochip hydrogel biomol detection

IT Genetic element
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ERE (estrogen-responsive element); three dimensional format biochips)

IT Antibodies and Immunoglobulins
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(IgG; three dimensional format biochips)

IT Prostate-specific antigen
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibodies to; three dimensional format biochips)

IT Polyoxyalkylenes, uses
RL: DEV (Device component use); USES (Uses)
(copolymers; three dimensional format biochips)

IT DNA
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(double-stranded; three dimensional format biochips)

IT **Immunoassay**
(enzyme-linked immunosorbent assay; three dimensional format biochips)

IT Albumins, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(serum, bovine; three dimensional format biochips)

IT Brain
Conformation
Dephosphorylation, biological
Diffusion
Electric field
Human
Molecular association
Nucleic acid hybridization
Phosphorylation
Viscosity
pH
(three dimensional format biochips)

IT Antigens
Transferrins
RL: ANT (Analyte); ANST (Analytical study)
(three dimensional format biochips)

IT Ferritins
RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(three dimensional format biochips)

IT Proteins
RL: ARU (Analytical role, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); ANST (Analytical study); PROC (Process)
(three dimensional format biochips)

IT Calmodulins
Estrogen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(three dimensional format biochips)

IT Chelates
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(three dimensional format biochips)

IT Enzymes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(three dimensional format biochips)

IT Peptides, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(three dimensional format biochips)

IT Receptors
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(three dimensional format biochips)
IT Antibodies and Immunoglobulins
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(three dimensional format biochips)
IT Macroglobulins
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(.alpha.2-; three dimensional format biochips)
IT 79747-53-8, Yersinia outer membrane protein 2b 81156-93-6 106436-17-3
117592-22-0 118447-68-0 127212-49-1 129785-85-9 149261-42-7
150268-17-0 151419-98-6 166664-90-0 176042-83-4 198754-34-6
300857-98-1, Leukocyte antigen related **protein tyrosine phosphatase** 444166-73-8 444166-74-9 444166-75-0
444166-76-1 444166-77-2 444166-78-3 444166-79-4
RL: ANT (Analyte); ANST (Analytical study)
(three dimensional format biochips)
IT 9002-07-7, Trypsin 444166-80-7
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(three dimensional format biochips)
IT 11128-99-7, Angiotensin II 361540-77-4, Calcineurin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(three dimensional format biochips)
IT 59828-41-0, HYPOL
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(three dimensional format biochips)
IT 124-38-9, Carbon dioxide, processes
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PROC (Process)
(three dimensional format biochips)
IT 25322-68-3D, Polyethylene glycol, copolymers 25322-69-4D, Polypropylene glycol, copolymers 181057-68-1, HYPOL PreMA G-50
RL: DEV (Device component use); USES (Uses)
(three dimensional format biochips)
IT 444272-42-8 444272-43-9 444272-44-0
RL: PRP (Properties)
(unclaimed sequence; three dimensional format biochips)

L25 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:408826 HCAPLUS
DN 137:5025
ED Entered STN: 31 May 2002
TI T cell **protein tyrosine phosphatase** inhibitors and activators for development of treatments for hematologic malignancies and autoimmune diseases
IN McGlade, Jane C.; Simoncic, Paul Daniel; Tremblay, Michael
PA The Hospital for Sick Children, Can.; McGill University
SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12Q001-42
ICS G01N033-566; G01N033-68; A61K038-47; A61P037-04; A61P037-06; G01N033-573
CC 15-10 (Immunochemistry)
Section cross-reference(s): 1, 3, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002042489	A1	20020530	WO 2001-CA1679	20011127 <--
WO 2002042489	C2	20021031		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002020412	A5	20020603	AU 2002-20412	20011127 <--

PRAI CA 2000-2326952 A 20001127 <--
WO 2001-CA1679 W 20011127

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002042489	ICM	C12Q001-42
	ICS	G01N033-566; G01N033-68; A61K038-47; A61P037-04; A61P037-06; G01N033-573

AB This invention relates to T cell **protein tyrosine phosphatase** (TCPTP) and more particularly to its role in cell signaling and interaction with the JAK family of tyrosine kinases. In particular, the invention involves the use of TCPTP for the development of treatments for malignancies and autoimmune conditions involving inappropriate JAK kinase signaling as well as for the identification of inhibitors and activators of this phosphatase. The invention may also be used to rule out TCPTP inhibition in selecting potential anti-diabetic and anti-obesity PTP1B inhibitors without immune suppression.

ST T cell **protein tyrosine phosphatase** hematol malignancy; autoimmune disease T cell **protein tyrosine phosphatase**; JAK kinase T cell signaling immunosuppressant

IT Antitumor agents
Autoimmune disease
Dephosphorylation, biological
Drug design
Drug screening
Hematopoietic precursor cell
Peptidomimetics
Phosphorylation, biological
Signal transduction, biological
T cell (lymphocyte)
Transplant and Transplantation
(T cell **protein tyrosine phosphatase** inhibitors and activators for development of treatments for hematol. malignancies and autoimmune diseases)

IT Fusion proteins (chimeric proteins)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(T cell **protein tyrosine phosphatase** inhibitors and activators for development of treatments for hematol. malignancies and autoimmune diseases)

IT Antisense oligonucleotides
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(T cell **protein tyrosine phosphatase** inhibitors and activators for development of treatments for hematol. malignancies and autoimmune diseases)

IT Gene, animal
Proteins
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(TCPTP; T cell **protein tyrosine phosphatase** inhibitors and activators for development of treatments for hematol. malignancies and autoimmune diseases)

IT Nucleic acids
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antisense; T cell **protein tyrosine phosphatase** inhibitors and activators for development of treatments for hematol. malignancies and autoimmune diseases)

IT Drug delivery systems
(carriers; T cell **protein tyrosine phosphatase** inhibitors and activators for development of treatments for hematol. malignancies and autoimmune diseases)

IT Lymphocyte
(disease, proliferation defect; T cell **protein tyrosine phosphatase** inhibitors and activators for development of treatments for hematol. malignancies and autoimmune diseases)

IT Hematopoiesis
(disorders; T cell **protein tyrosine phosphatase** inhibitors and activators for development of treatments for hematol. malignancies and autoimmune diseases)

IT Neoplasm
(hematol.; T cell **protein tyrosine phosphatase** inhibitors and activators for development of treatments for hematol. malignancies and autoimmune diseases)

IT Antidiabetic agents
Antiobesity agents
(immunosuppression examination; T cell **protein tyrosine phosphatase** inhibitors and activators for development of treatments for hematol. malignancies and autoimmune diseases)
IT Carbohydrates, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(metabolism; T cell **protein tyrosine phosphatase** inhibitors and activators for development of treatments for hematol. malignancies and autoimmune diseases)
IT Diabetes mellitus
(resistance; T cell **protein tyrosine phosphatase** inhibitors and activators for development of treatments for hematol. malignancies and autoimmune diseases)
IT Anti-inflammatory agents
Immunostimulants
Immunosuppressants
(screening; T cell **protein tyrosine phosphatase** inhibitors and activators for development of treatments for hematol. malignancies and autoimmune diseases)
IT Mutagenesis
(site-directed, deletion; T cell **protein tyrosine phosphatase** inhibitors and activators for development of treatments for hematol. malignancies and autoimmune diseases)
IT Mutagenesis
(site-directed; T cell **protein tyrosine phosphatase** inhibitors and activators for development of treatments for hematol. malignancies and autoimmune diseases)
IT 152478-56-3, JAK1 kinase 157482-36-5, JAK3 kinase 161384-16-3, JAK kinase
RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(T cell **protein tyrosine phosphatase** inhibitors and activators for development of treatments for hematol. malignancies and autoimmune diseases)
IT 300842-01-7, T Cell **Protein tyrosine phosphatase**
RL: ANT (Analyte); ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(inhibitor and activator; T cell **protein tyrosine phosphatase** inhibitors and activators for development of treatments for hematol. malignancies and autoimmune diseases)
IT 60-18-4, Tyrosine, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phosphorylation; T cell **protein tyrosine phosphatase** inhibitors and activators for development of treatments for hematol. malignancies and autoimmune diseases)
IT 432838-28-3 432838-29-4 432838-30-7 432838-31-8 432838-32-9
432838-33-0 432838-35-2 432838-36-3 432838-37-4 432838-38-5
432838-39-6 432838-40-9 432838-41-0
RL: PRP (Properties)
(unclaimed sequence; t cell **protein tyrosine phosphatase** inhibitors and activators for development of treatments for hematol. malignancies and autoimmune diseases)
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Df Jesus, I; WO 0036111 A 2000
(2) Flint, A; PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES 1997, V94(5), P1680 HCAPLUS
(3) Gjorloff-Wingren, A; EUROPEAN JOURNAL OF IMMUNOLOGY 2000, V30(8), P2412 HCAPLUS
(4) Hui, Z; WO 0075339 A 2000 HCAPLUS
(5) Ibarra-Sanchez, M; SEMIN IMMUNOL 2000, V12(4), P379 HCAPLUS
(6) Ihle, J; SEMIN IMMUNOLOGY 1995, V7, P247 HCAPLUS
(7) Lp, H; WO 9936548 A 1999 HCAPLUS
(8) Maegawa, H; BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS 1996, V228(1), P122 HCAPLUS
(9) Maegawa, H; JOURNAL OF BIOLOGICAL CHEMISTRY 1999, V274(42), P30236 HCAPLUS
(10) Novo Nordisk As; WO 0117516 A 2001 HCAPLUS
(11) Sugen Inc; WO 9827092 A 1998 HCAPLUS
(12) Tiganis, T; JOURNAL OF BIOLOGICAL CHEMISTRY 1997, V272(34), P21548 HCAPLUS
(13) Tiganis, T; MOLECULAR AND CELLULAR BIOLOGY 1998, V18(3), P1622 HCAPLUS
(14) Univ Rockefeller; WO 9923493 A 1999 HCAPLUS
(15) Wimmer, M; HISTOCHEMISTRY AND CELL BIOLOGY 1999, V111(2), P135 HCAPLUS
(16) You-Ten, K; JOURNAL OF EXPERIMENTAL MEDICINE 1997, V186(5), P683 HCAPLUS

L25 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:618190 HCAPLUS
DN 135:207447
ED Entered STN: 24 Aug 2001
TI Fluorescent assay for **protein tyrosine phosphatases**
IN Flint, Andrew J.; Cool, Deborah E.
PA Ceptyr, Inc., USA
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12Q001-00
CC 7-1 (Enzymes)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001061031	A2	20010823	WO 2001-US5180	20010213 <--
	WO 2001061031	A3	20020307		
	WO 2001061031	C2	20021017		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002009762	A1	20020124	US 2001-788626	20010213 <--
	EP 1257824	A2	20021120	EP 2001-910900	20010213 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	US 2000-181769P	P	20000214 <--		
	WO 2001-US5180	W	20010213		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001061031	ICM	C12Q001-00

AB The invention relates in part to screening assays for identifying agents that alter the interaction between a **protein tyrosine phosphatase** (PTP) and its tyrosine phosphorylated polypeptide substrate, using fluorescence energy signals generated by detectably labeled substrates. Assays are provided in certain embodiments, including high throughput screening assays, wherein candidate agents are screened by fluorescence polarization for their ability to influence (i) binding of substrate trapping mutant PTPs to substrates, or (ii) dephosphorylation of tyrosine phosphorylated substrates by PTPs.
ST **protein tyrosine phosphatase** detn
fluorescence polarization
IT Phosphoproteins
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(P210bcr-c-abl, phosphopeptide derived from; fluorescent assay for **protein tyrosine phosphatases**)
IT Protein motifs
(PH domain, polypeptide containing, reaction terminator; fluorescent assay for **protein tyrosine phosphatases**)
IT Protein motifs
(PTB domain, polypeptide containing, reaction terminator; fluorescent assay for **protein tyrosine phosphatases**)
IT Protein motifs
(PTB-PID domain, polypeptide containing, reaction terminator; fluorescent assay for **protein tyrosine phosphatases**)
IT Protein motifs
(SH2 domain, polypeptide containing, reaction terminator; fluorescent assay for **protein tyrosine phosphatases**)
IT Phosphoproteins
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(SHC, phosphopeptide derived from; fluorescent assay for **protein tyrosine phosphatases**)
IT Proteins, specific or class
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(VCP, phosphopeptide derived from; fluorescent assay for **protein tyrosine phosphatases**)
IT Enzyme functional sites

(active; fluorescent assay for **protein tyrosine phosphatases**)
IT Resonant energy transfer
(fluorescence; fluorescent assay for **protein tyrosine phosphatases**)
IT **Dephosphorylation, biological**
Fluorescence
Fluorescent substances
Polarized fluorescence
(fluorescent assay for **protein tyrosine phosphatases**)
IT CD45 (antigen)
RL: ANT (Analyte); ANST (Analytical study)
(fluorescent assay for **protein tyrosine phosphatases**)
IT Phosphopeptides
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(fluorescent assay for **protein tyrosine phosphatases**)
IT **Drug screening**
(fluorescent assay for **protein tyrosine phosphatases** in relation to)
IT Proteins, specific or class
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(p130, p130cas, phosphopeptide derived from; fluorescent assay for **protein tyrosine phosphatases**)
IT Epidermal growth factor receptors
Insulin receptors
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(phosphopeptide derived from; fluorescent assay for **protein tyrosine phosphatases**)
IT Phosphoproteins
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(pp56lck, phosphopeptide derived from; fluorescent assay for **protein tyrosine phosphatases**)
IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(reaction terminator; fluorescent assay for **protein tyrosine phosphatases**)
IT Mutation
(substitution, of **protein tyrosine phosphatase**; fluorescent assay for **protein tyrosine phosphatases**)
IT TCR (T cell receptors)
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(zeta chain, phosphopeptide derived from; fluorescent assay for **protein tyrosine phosphatases**)
IT 60-18-4, L-Tyrosine, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(-676, phosphatase wild-type Tyr replaced by; fluorescent assay for **protein tyrosine phosphatases**)
IT 247144-99-6, Alexa Fluor 488
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(Alexa Fluor 488, fluorophore; fluorescent assay for **protein tyrosine phosphatases**)
IT 247145-86-4, Alexa Fluor 594
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(Alexa Fluor 594, fluorophore; fluorescent assay for **protein tyrosine phosphatases**)
IT 146368-14-1
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(Cy5, fluorophore; fluorescent assay for **protein tyrosine phosphatases**)
IT 330956-25-7, Leukocyte **protein tyrosine phosphatase**
RL: ANT (Analyte); ANST (Analytical study)
(LC-PTP, reaction terminator; fluorescent assay for **protein tyrosine phosphatases**)
IT 79747-53-8, **Protein tyrosine phosphatase**
196717-98-3, **protein tyrosine phosphatase** PEST 300830-54-0, PTP-MEG1 300842-01-7, TC-PTP 300857-98-1, **Protein tyrosine phosphatase** LAR
300865-11-6, **protein tyrosine phosphatase** 1B
300865-18-3, **Protein tyrosine phosphatase** .mu. 300865-46-7, **Protein tyrosine phosphatase** .gamma. 301156-53-6, **Protein**

tyrosine phosphatase SHP2 301162-72-1, **Protein tyrosine phosphatase** H1 306298-47-5, MAPK phosphatase 1
RL: ANT (Analyte); ANST (Analytical study)
(fluorescent assay for **protein tyrosine phosphatases**)

IT 76823-03-5DP, 5-Carboxyfluorescein, reaction products with phosphopeptides 207554-36-7DP, reaction products with fluorescein 357164-39-7DP, reaction products with fluorescein 357164-40-0DP, reaction products with fluorescein
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(fluorescent assay for **protein tyrosine phosphatases**)

IT 2321-07-5, Fluorescein 13558-31-1 82354-19-6, Texas Red 165599-63-3, BODIPY-FL
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(fluorophore; fluorescent assay for **protein tyrosine phosphatases**)

IT 52-90-4, L-Cysteine, analysis 56-40-6, Glycine, analysis 56-41-7, L-Alanine, analysis 56-84-8, L-Aspartic acid, analysis 56-85-9, L-Glutamine, analysis 56-86-0, L-Glutamic acid, analysis 56-87-1, L-Lysine, analysis 61-90-5, L-Leucine, analysis 63-68-3, L-Methionine, analysis 63-91-2, L-Phenylalanine, analysis 70-47-3, L-Asparagine, analysis 71-00-1, L-Histidine, analysis 72-18-4, L-Valine, analysis 73-22-3, L-Tryptophane, analysis 73-32-5, L-Isoleucine, analysis 74-79-3, L-Arginine, analysis 147-85-3, L-Proline, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(phosphatase wild-type Tyr replaced by; fluorescent assay for **protein tyrosine phosphatases**)

IT 114051-78-4, Lck tyrosine kinase
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(phosphopeptide derived from; fluorescent assay for **protein tyrosine phosphatases**)

IT 300854-55-1, PTP-DEP1 300859-91-0, PTP-CD45 356771-02-3 356771-72-7 356771-80-7
RL: ANT (Analyte); ANST (Analytical study)
(reaction terminator; fluorescent assay for **protein tyrosine phosphatases**)

IT 37353-31-4, vanadate
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(reaction terminator; fluorescent assay for **protein tyrosine phosphatases**)

IT 142243-02-5, MAP kinase
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(substrate phosphopeptide derived from; fluorescent assay for **protein tyrosine phosphatases**)

IT 313285-28-8 313285-34-6 313285-39-1 357464-46-1 357464-47-2
357464-48-3 357464-49-4 357464-50-7 357464-51-8 357464-52-9
357464-53-0 357464-54-1 357464-55-2 357464-56-3 357464-57-4
357464-58-5 357464-59-6 357464-60-9 357464-61-0 357464-62-1
357464-63-2 357464-64-3 357464-65-4 357464-66-5 357464-67-6
357464-68-7 357464-69-8 357464-70-1 357464-71-2 357464-72-3
357464-73-4 357464-74-5 357464-75-6 357464-76-7 357464-77-8
RL: PRP (Properties)
(unclaimed sequence; fluorescent assay for **protein tyrosine phosphatases**)

L25 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:582074 HCAPLUS
DN 135:163001
ED Entered STN: 10 Aug 2001
TI Interaction of NMDA receptor with **protein tyrosine phosphatase**, screening for agents which modulate NMDA receptor signaling, and therapeutic applications
IN Melcher, Thorsten; Kask, Kalev
PA Agy Therapeutics, Inc., USA
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12Q001-00
CC 2-8 (Mammalian Hormones)
Section cross-reference(s): 1, 7, 63
FAN.CNT 3
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	WO 2001057240	A2	20010809	WO 2001-US3049	20010130 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1255854	A2	20021113	EP 2001-908752	20010130 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003521247	T2	20030715	JP 2001-555863	20010130 <--
PRAI	US 2000-179453P	P	20000201 <--		
	WO 2001-US3049	W	20010130		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001057240	ICM	C12Q001-00

AB The present invention relates to the identification of a binding between NMDA receptor (NMDA-R) subunits and a **protein tyrosine phosphatase** (PTP), e.g., PTPL1. The present invention provides methods for screening a PTP agonist or antagonist that modulates NMDA-R signaling. The present invention also provide methods and compns. for treatment of disorders mediated by abnormal NMDA-R signaling. The present invention further provides methods for isolating PTPL1 from a biol. preparation

ST NMDA receptor **protein tyrosine phosphatase** PTPL1 therapeutic; drug screening NMDA receptor **protein tyrosine phosphatase** PTPL1

IT Nervous system
(Huntington's chorea, treatment of; interaction of NMDA receptor with **protein tyrosine phosphatase** PTPL1, screening for agents which modulate NMDA receptor signaling, and therapeutic applications)

IT Gene, animal
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(NMDA receptor signaling modulator-encoding; interaction of NMDA receptor with **protein tyrosine phosphatase** PTPL1, screening for agents which modulate NMDA receptor signaling, and therapeutic applications)

IT Glutamate receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(NMDA-binding; interaction of NMDA receptor with **protein tyrosine phosphatase** PTPL1, screening for agents which modulate NMDA receptor signaling, and therapeutic applications)

IT Mental disorder
(dementia, treatment of; interaction of NMDA receptor with **protein tyrosine phosphatase** PTPL1, screening for agents which modulate NMDA receptor signaling, and therapeutic applications)

IT Analgesics
(for chronic pain treatment; interaction of NMDA receptor with **protein tyrosine phosphatase** PTPL1, screening for agents which modulate NMDA receptor signaling, and therapeutic applications)

IT Brain, disease
(injury, treatment of; interaction of NMDA receptor with **protein tyrosine phosphatase** PTPL1, screening for agents which modulate NMDA receptor signaling, and therapeutic applications)

IT Anti-Alzheimer's agents
Anticonvulsants
Antipsychotics
Dephosphorylation, biological
Drug screening
Drugs
Molecular association
Signal transduction, biological
(interaction of NMDA receptor with **protein tyrosine phosphatase** PTPL1, screening for agents which modulate NMDA receptor signaling, and therapeutic applications)

IT Nerve, disease

(motor, treatment of; interaction of NMDA receptor with **protein tyrosine phosphatase** PTPL1, screening for agents which modulate NMDA receptor signaling, and therapeutic applications)
IT Nerve, disease
(neuropathy, treatment of; interaction of NMDA receptor with **protein tyrosine phosphatase** PTPL1, screening for agents which modulate NMDA receptor signaling, and therapeutic applications)
IT Phosphorylation, biological
(protein; interaction of NMDA receptor with **protein tyrosine phosphatase** PTPL1, screening for agents which modulate NMDA receptor signaling, and therapeutic applications)
IT Nervous system
(spinocerebellar degeneration, treatment of; interaction of NMDA receptor with **protein tyrosine phosphatase** PTPL1, screening for agents which modulate NMDA receptor signaling, and therapeutic applications)
IT Brain, disease
(stroke, treatment of; interaction of NMDA receptor with **protein tyrosine phosphatase** PTPL1, screening for agents which modulate NMDA receptor signaling, and therapeutic applications)
IT Head
(trauma, treatment of; interaction of NMDA receptor with **protein tyrosine phosphatase** PTPL1, screening for agents which modulate NMDA receptor signaling, and therapeutic applications)
IT Alcoholism
Drug dependence
Schizophrenia
(treatment of; interaction of NMDA receptor with **protein tyrosine phosphatase** PTPL1, screening for agents which modulate NMDA receptor signaling, and therapeutic applications)
IT 79747-53-8P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(L1 isoenzyme; interaction of NMDA receptor with **protein tyrosine phosphatase** PTPL1, screening for agents which modulate NMDA receptor signaling, and therapeutic applications)

L25 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:251041 HCAPLUS
DN 133:70565
ED Entered STN: 19 Apr 2000
TI Structure-based design of a low molecular weight, nonphosphorus, nonpeptide, and highly selective inhibitor of **protein-tyrosine phosphatase** 1B
AU Iversen, Lars Fogh; Andersen, Henrik Sune; Branner, Sven; Mortensen, Steen B.; Peters, Gunther H.; Norris, Kjeld; Olsen, Ole Hvilsted; Jeppesen, Claus Bekker; Lundt, Behrend F.; Ripka, William; Moller, Karin Bach; Moller, Niels Peter Hundahl
CS Protein Chemistry, Bagsvaerd, DK-2880, Den.
SO Journal of Biological Chemistry (**2000**), 275(14), 10300-10307
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 7-3 (Enzymes)
Section cross-reference(s): 1, 75
AB Several **protein-tyrosine phosphatases** (PTPs) have been proposed to act as neg. regulators of insulin signaling. Recent studies have shown increased insulin sensitivity and resistance to obesity in PTP1B knockout mice, thus pointing to this enzyme as a potential drug target in diabetes. Structure-based design, guided by PTP mutants and x-ray protein crystallog., was used to optimize a relatively weak, nonphosphorus, nonpeptide general PTP inhibitor (2-(oxalyl-amino)-benzoic acid) into a highly selective PTP1B inhibitor. This was achieved by addressing residue 48 as a selectivity determining residue. By introducing a basic nitrogen in the core structure of the inhibitor, a salt bridge was formed to Asp-48 in PTP1B. In contrast, the basic nitrogen causes repulsion in other PTPs containing an asparagine in the equivalent position resulting in a remarkable selectivity for PTP1B. Importantly, this was accomplished while retaining the mol. weight of the inhibitor below 300 g/mol.

ST **protein tyrosine phosphatase** 1B inhibitor oxalylaminobenzoate; crystal structure **protein tyrosine phosphatase** 1B

IT Enzyme functional sites
(active; structure-based design of a low mol. weight, nonphosphorus, nonpeptide, and highly selective inhibitor of **protein-tyrosine phosphatase** 1B)

IT Structure-activity relationship
(enzyme-inhibiting; structure-based design of a low mol. weight, nonphosphorus, nonpeptide, and highly selective inhibitor of **protein-tyrosine phosphatase** 1B)

IT Enzyme kinetics
(of inhibition; structure-based design of a low mol. weight, nonphosphorus, nonpeptide, and highly selective inhibitor of **protein-tyrosine phosphatase** 1B)

IT Conformation
(protein; structure-based design of a low mol. weight, nonphosphorus, nonpeptide, and highly selective inhibitor of **protein-tyrosine phosphatase** 1B)

IT Conformational transition
Crystal structure
Dephosphorylation, biological
Drug design
(structure-based design of a low mol. weight, nonphosphorus, nonpeptide, and highly selective inhibitor of **protein-tyrosine phosphatase** 1B)

IT 79747-53-8
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(1B; structure-based design of a low mol. weight, nonphosphorus, nonpeptide, and highly selective inhibitor of **protein-tyrosine phosphatase** 1B)

IT 79747-53-8D, complexes with oxalylaminobenzoate-based derivs.
RL: PRP (Properties)
(1B; structure-based design of a low mol. weight, nonphosphorus, nonpeptide, and highly selective inhibitor of **protein-tyrosine phosphatase** 1B)

IT 5651-01-4 243966-03-2 243967-41-1 243967-42-2 243985-35-5 243985-58-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(structure-based design of a low mol. weight, nonphosphorus, nonpeptide, and highly selective inhibitor of **protein-tyrosine phosphatase** 1B)

IT 243967-41-1D, complexes with **protein-tyrosine phosphatase** 1B 243967-42-2D, complexes with **protein-tyrosine phosphatase** 1B
RL: PRP (Properties)
(structure-based design of a low mol. weight, nonphosphorus, nonpeptide, and highly selective inhibitor of **protein-tyrosine phosphatase** 1B)

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L25 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:185782 HCAPLUS
DN 132:344765
ED Entered STN: 23 Mar 2000
TI 2-(Oxalylamino)-benzoic acid is a general, competitive inhibitor of **protein-tyrosine phosphatases**
AU Andersen, Henrik Sune; Iversen, Lars Fogh; Jeppesen, Claus Bekker; Branner, Sven; Norris, Kjeld; Rasmussen, Hanne B.; Moller, Karin Bach; Moller, Niels Peter Hundahl
CS MedChem Research I, Bagsvaerd, DK-2880, Den.
SO Journal of Biological Chemistry (**2000**), 275(10), 7101-7108
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 7-3 (Enzymes)
Section cross-reference(s): 1, 75
AB **Protein-tyrosine phosphatases** (PTPs) are critically involved in regulation of signal transduction processes. Members of this class of enzymes are considered attractive therapeutic targets in several disease states, e.g. diabetes, cancer, and inflammation. However, most reported PTP inhibitors have been phosphorus-containing compds., tight binding inhibitors, and/or inhibitors that covalently modify the enzymes. We therefore embarked on identifying a general, reversible, competitive PTP inhibitor that could be used as a common scaffold for lead optimization for specific PTPs. We here report the identification of 2-(oxalylamino)-benzoic acid (OBA) as a classical competitive inhibitor of several PTPs. X-ray crystallog. of PTP1B complexed with OBA and related non-phosphate low mol. weight derivs. reveals that the binding mode of these mols. to a large extent mimics that of the natural substrate including hydrogen bonding to the PTP signature motif. In addition, binding of OBA to the active site of PTP1B creates a unique arrangement involving Asp181, Lys120, and Tyr46. PTP inhibitors are essential tools in elucidating the biol. function of specific PTPs and they may eventually be developed into selective drug candidates. The unique enzyme kinetic features and the low mol. weight of OBA makes it an ideal starting point for further optimization.
ST **protein tyrosine phosphatase** inhibitor oxalylaminobenzoate drug design; crystal structure **protein tyrosine phosphatase** inhibitor
IT Conformation
Conformational transition
Crystal structure
Dephosphorylation, biological
Drug design
Ionization
(2-(oxalylamino)-benzoic acid is a general, competitive inhibitor of **protein-tyrosine phosphatases**)
IT Enzyme functional sites
(active; 2-(oxalylamino)-benzoic acid is a general, competitive inhibitor of **protein-tyrosine phosphatases**
)
IT Enzyme kinetics
(of inhibition; 2-(oxalylamino)-benzoic acid is a general, competitive

inhibitor of **protein-tyrosine phosphatases**
)
IT 5651-01-4, 2-(Oxalylamino)-benzoic acid 243967-43-3 243967-44-4
243989-49-3 243989-50-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(2-(oxalylamino)-benzoic acid is a general, competitive inhibitor of **protein-tyrosine phosphatases**)
IT 5651-01-4D, 2-(Oxalylamino)-benzoic acid, complexes with **protein-tyrosine phosphatases** 79747-53-8D, **Protein tyrosine phosphatase**, complexes with oxalylaminobenzoate and derivs. 243967-44-4D, complexes with **protein-tyrosine phosphatases** 243989-49-3D, complexes with **protein-tyrosine phosphatases** 243989-50-6D, complexes with **protein-tyrosine phosphatases**
RL: PRP (Properties)
(2-(oxalylamino)-benzoic acid is a general, competitive inhibitor of **protein-tyrosine phosphatases**)
IT 79747-53-8, **Protein tyrosine phosphatase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(multiple forms of; 2-(oxalylamino)-benzoic acid is a general, competitive inhibitor of **protein-tyrosine phosphatases**)
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L25 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:101696 HCAPLUS
DN 132:304951
ED Entered STN: 13 Feb 2000

TI 3,6-Fluorescein diphosphate: a sensitive fluorogenic and chromogenic substrate for **protein tyrosine phosphatases**

AU Huang, Zheng; Wang, Qingping; Ly, Hoa D.; Gorvindarajan, Arvind; Scheigetz, John; Zamboni, Robert; Desmarais, Sylvie; Ramachandran, Chidambaram

CS Merck Frosst Center for Therapeutic Research, Dorval, QC, Can.

SO Journal of Biomolecular Screening (**1999**), 4(6), 327-334
CODEN: JBISF3; ISSN: 1087-0571

PB Mary Ann Liebert, Inc.

DT Journal

LA English

CC 7-1 (Enzymes)
Section cross-reference(s): 1

AB A highly sensitive and continuous **protein tyrosine phosphatase** (PTPase) assay using 3,6-fluorescein diphosphate (FDP) is described. Leukocyte phosphatase CD45 (leukocyte common antigen), **protein tyrosine phosphatase**-1B, and leukocyte common antigen-related protein LAR preferentially hydrolyze FDP to fluorescein monophosphate (FMP) with Vmax and Km values comparable with those of phosphotyrosine peptide substrates. Further hydrolysis of FMP to fluorescein was less efficient because of increased Km values compared with those of FDP. FMP absorbs strongly at 445 nm and fluoresces intensely near 515 nm, both of which are insensitive to pH perturbations above pH 6. Its high catalytic efficiency, coupled with the highly sensitive dual detection in the visible wavelength region and wider pH operating range, make FDP the substrate of choice for PTPase inhibitor screening in HTS format and assay miniaturization.

ST **protein tyrosine phosphatase** substrate
fluorescein diphosphate

IT **Dephosphorylation, biological**
Drug screening
Fluorescence
Michaelis constant
(3,6-fluorescein diphosphate is a sensitive fluorogenic and chromogenic substrate for **protein tyrosine phosphatases**
)

IT 79747-53-8, **Protein tyrosine phosphatase**
RL: ANT (Analyte); ANST (Analytical study)
(3,6-fluorescein diphosphate is a sensitive fluorogenic and chromogenic substrate for **protein tyrosine phosphatases**
)

IT 134869-03-7, 3,6-Fluorescein diphosphate
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(3,6-fluorescein diphosphate is a sensitive fluorogenic and chromogenic substrate for **protein tyrosine phosphatases**
)

IT 185252-56-6
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(3,6-fluorescein diphosphate is a sensitive fluorogenic and chromogenic substrate for **protein tyrosine phosphatases**
)

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L25 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:356398 HCAPLUS
DN 131:196127
ED Entered STN: 10 Jun 1999
TI Microtiter Well Assays for **Protein Tyrosine Phosphatase** Activities Directed against Phosphorylated Insulin Receptor or Insulin Receptor Substrate-1
AU Krutzfeldt, Jan; Grunweller, Arnold; Raasch, Walter; Drenckhan, Maren; Klein, Harald H.
CS Department of Internal Medicine 1, Medical University of Lubeck, Lubeck, D-23538, Germany
SO Analytical Biochemistry (**1999**), 271(1), 97-99
CODEN: ANBCA2; ISSN: 0003-2697
PB Academic Press
DT Journal
LA English
CC 7-1 (Enzymes)
AB A microwell-based assay system was developed that allows one to specifically measure **protein tyrosine phosphatase** (PTPase) activities directed against two proteins involved in insulin signaling. It represents a useful tool for the investigation of potential alterations in PTPase activities in different states of insulin resistance. Moreover, similar assays can be established for other membrane-bound and cytosolic tyrosine-phosphorylated proteins. (c) 1999 Academic Press.
ST microtiter assay **protein tyrosine phosphatase** insulin receptor substrate
IT Phosphoproteins
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(IRS-1 (insulin receptor substrate 1), phosphorylated, immobilized; microtiter well assays for **protein tyrosine phosphatase** activities directed against phosphorylated insulin receptor or insulin receptor substrate-1)
IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(biotinylated, against phosphotyrosine; microtiter well assays for **protein tyrosine phosphatase** activities directed against phosphorylated insulin receptor or insulin receptor substrate-1)
IT **Immunoassay**
(enzyme-linked immunosorbent assay; microtiter well assays for **protein tyrosine phosphatase** activities directed against phosphorylated insulin receptor or insulin receptor substrate-1)
IT **Dephosphorylation, biological**
(microtiter well assays for **protein tyrosine phosphatase** activities directed against phosphorylated insulin receptor or insulin receptor substrate-1)
IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(monoclonal, against insulin receptor or insulin receptor substrate-1; microtiter well assays for **protein tyrosine phosphatase** activities directed against phosphorylated insulin receptor or insulin receptor substrate-1)
IT Insulin receptors
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(phosphorylated, immobilized; microtiter well assays for **protein tyrosine phosphatase** activities directed against phosphorylated insulin receptor or insulin receptor substrate-1)
IT 79747-53-8, **Protein tyrosine phosphatase**
RL: ANT (Analyte); ANST (Analytical study)
(microtiter well assays for **protein tyrosine phosphatase** activities directed against phosphorylated insulin receptor or insulin receptor substrate-1)
IT 9003-99-0D, Peroxidase, conjugates with streptavidin 9013-20-1D, Streptavidin, conjugates with horseradish peroxidase 28752-68-3, ABTS
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(microtiter well assays for **protein tyrosine**

phosphatase activities directed against phosphorylated insulin receptor or insulin receptor substrate-1)

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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(5) Hauguel-de Mouzon, S; Endocrinology 1993, V132, P67 HCAPLUS
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L25 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:550508 HCAPLUS
DN 129:187420
ED Entered STN: 31 Aug 1998
TI Tyrosine phosphorylated proteins (PSTPIPs) found in the cleavage furrow that are substrates for PEST **protein tyrosine phosphatases**
IN Lasky, Laurence A.; Dowbenko, Donald J.
PA Genentech, Inc., USA
SO PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-12
ICS C07K014-47; G01N033-50; C07K016-18; C12N005-20
CC 13-3 (Mammalian Biochemistry)
Section cross-reference(s): 6
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9835037	A1	19980813	WO 1998-US1774	19980130	<--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	ZA 9800651	A	19990727	ZA 1998-651	19980127	<--
	AU 9866493	A1	19980826	AU 1998-66493	19980130	<--
	AU 731570	B2	20010405			
	EP 980426	A1	20000223	EP 1998-908458	19980130	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	JP 2001503994	T2	20010327	JP 1998-534800	19980130	<--
	JP 3503951	B2	20040308			
	MX 9907114	A	20000228	MX 1999-7114	19990730	<--
PRAI	US 1997-798419	A	19970207	<--		
	US 1997-938829	A2	19970929	<--		
	WO 1998-US1774	W	19980130	<--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9835037	ICM	C12N015-12
	ICS	C07K014-47; G01N033-50; C07K016-18; C12N005-20
WO 9835037	ECLA	C07K014/47 <--

AB Novel proteins that are substrates for dephosphorylation by the PEST family of **protein tyrosine phosphatases** and that are associated with the cleavage furrow are described and cDNAs encoding them are cloned from mouse. The protein appears to play a role in the polymerization of actin and so may be a target for the control of the process. The protein was identified as a ligand for PTP PEST in a yeast two-hybrid system using a cDNA bank from mouse Baf3 cells. The protein was found in actin-rich sites within the cell, specifically with the cortical actin cytoskeleton.

ST PSTPIP actin polymn cytokinesis; tyrosine dephosphorylation PSTPIP PTP PEST; cDNA PSTPIP mouse; cleavage furrow PSTPIP

IT Cytoskeleton
(PSTPIP association with cortical actin of; tyrosine phosphorylated proteins (PSTPIPs) found in cleavage furrow that are substrates for PEST **protein tyrosine phosphatases**)
IT Actins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(PSTPIP interaction with; tyrosine phosphorylated proteins (PSTPIPs) found in cleavage furrow that are substrates for PEST **protein tyrosine phosphatases**)
IT Embryo, animal
(PSTPIP levels in, as function of developmental stage; tyrosine phosphorylated proteins (PSTPIPs) found in cleavage furrow that are substrates for PEST **protein tyrosine phosphatases**)
IT Phosphoproteins
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(PSTPIP; tyrosine phosphorylated proteins (PSTPIPs) found in cleavage furrow that are substrates for PEST **protein tyrosine phosphatases**)
IT Protein motifs
(SH3 domain, in PSTPIP; tyrosine phosphorylated proteins (PSTPIPs) found in cleavage furrow that are substrates for PEST **protein tyrosine phosphatases**)
IT Gene, animal
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(cDNA, for PSTPIP of mouse; tyrosine phosphorylated proteins (PSTPIPs) found in cleavage furrow that are substrates for PEST **protein tyrosine phosphatases**)
IT Cell division
(cytokinesis, PSTPIP in cleavage furrow during; tyrosine phosphorylated proteins (PSTPIPs) found in cleavage furrow that are substrates for PEST **protein tyrosine phosphatases**)
IT **Drug screening**
(for effectors of PSTPIP-mediated actin polymerization; tyrosine phosphorylated proteins (PSTPIPs) found in cleavage furrow that are substrates for PEST **protein tyrosine phosphatases**)
IT cDNA sequences
(for phosphoprotein PSTPIP of mouse; tyrosine phosphorylated proteins (PSTPIPs) found in cleavage furrow that are substrates for PEST **protein tyrosine phosphatases**)
IT Antibodies
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(monoclonal, to PSTPIP; tyrosine phosphorylated proteins (PSTPIPs) found in cleavage furrow that are substrates for PEST **protein tyrosine phosphatases**)
IT Molecular association
(of PSTPIP and PTP PEST, characterization of; tyrosine phosphorylated proteins (PSTPIPs) found in cleavage furrow that are substrates for PEST **protein tyrosine phosphatases**)
IT Protein motifs
(of PSTPIP of mouse; tyrosine phosphorylated proteins (PSTPIPs) found in cleavage furrow that are substrates for PEST **protein tyrosine phosphatases**)
IT **Dephosphorylation, biological**
(of PSTPIP **proteins** by PEST **phosphatases**; **tyrosine** phosphorylated **proteins** (PSTPIPs) found in cleavage furrow that are substrates for PEST **protein tyrosine phosphatases**)
IT Protein sequences
(of phosphoprotein PSTPIP of mouse; tyrosine phosphorylated proteins (PSTPIPs) found in cleavage furrow that are substrates for PEST **protein tyrosine phosphatases**)
IT Antibodies
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(to PSTPIP; tyrosine phosphorylated proteins (PSTPIPs) found in cleavage furrow that are substrates for PEST **protein tyrosine phosphatases**)
IT 196523-73-6
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP

(Properties); BIOL (Biological study); OCCU (Occurrence)
(amino acid sequence, association with actin of; tyrosine phosphorylated proteins (PSTPIPs) found in cleavage furrow that are substrates for PEST **protein tyrosine phosphatases**)
IT 196717-98-3
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(dephosphorylation of PSTPIP by; tyrosine phosphorylated proteins (PSTPIPs) found in cleavage furrow that are substrates for PEST **protein tyrosine phosphatases**)
IT 211623-46-0
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; tyrosine phosphorylated proteins (PSTPIPs) found in cleavage furrow that are substrates for PEST **protein tyrosine phosphatases**)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L51 ANSWER 1 OF 11 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN **2003465693** EMBASE
TI Molecular Cloning and Characterization of a Novel Dual Specificity Phosphatase, LMW-DSP2, that Lacks the Cdc25 Homology Domain.
AU Aoyama K.; Nagata M.; Oshima K.; Matsuda T.; Aoki N.
CS . naoki@agr.nagoya-u.ac.jp
SO Journal of Biological Chemistry, (20 Jul 2001) 276/29 (27575-27583).
Refs: 46
ISSN: 0021-9258 CODEN: JBCHA3
CY United States
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
AB A novel dual specificity phosphatase (DSP) designated LMW-DSP2 was cloned with a combination of reverse transcription-polymerase chain reaction and cDNA library screening strategies. The LMW-DSP2 open reading frame of 194 amino acids contained a single DSP catalytic domain but lacked the cdc25 homology domain, which is conserved in most known DSPs. Northern blot and reverse transcription-polymerase chain reaction analyses revealed that LMW-DSP2 was specifically expressed in testis. Recombinant LMW-DSP2 protein exhibited phosphatase activity toward an artificial low molecular weight substrate paranitrophenyl phosphate, and the activity was inhibited completely by sodium orthovanadate but not sodium fluoride, pyrophosphate, and okadaic acid. The substitution of critical amino acid residues, aspartic acid and cysteine, resulted in a dramatic reduction of phosphatase activity. Transient transfection of LMW-DSP2 in COS7 cells resulted in the expression of a 21-kDa protein, and the phosphatase was shown to be distributed in both the cytosol and the nucleus. LMW-DSP2 dephosphorylated and deactivated p38, to a higher extent, and stress-activated protein kinase (SAPK)/c-Jun N-terminal kinase (JNK), but not extracellular signal-regulated kinase 1/2 mitogen-activated protein kinases, in transfected COS7 cells and in vitro. Interestingly, mutation in a conserved docking motif of p38 and SAPK/JNK as well as in a cluster of aspartic acids of LMW-DSP2 did not affect the deactivation of the mitogen-activated protein kinases by LMW-DSP2. Furthermore, the binding between LMW-DSP2 and p38 and SAPK/JNK was also not disrupted by such

mutations. Among the DSPs lacking the cdc25 homology domain, LMW-DSP2 is the first one that dephosphorylates and deactivates p38 and SAPK/JNK.

CT Medical Descriptors:
*molecular cloning
*enzyme specificity
*protein domain
*sequence homology
*nucleotide sequence
reverse transcription polymerase chain reaction
DNA library
genetic screening
open reading frame
amino acid analysis
Northern blotting
protein expression
testis
enzyme activity
molecular weight
enzyme substrate
amino acid substitution
genetic transfection
enzyme localization
cytosol
cell nucleus
enzyme inactivation
protein phosphorylation
in vitro study
protein motif
binding kinetics
binding affinity
gene mutation
nonhuman
controlled study
animal cell
article
priority journal
Drug Descriptors:
*phosphatase
*dual specificity phosphatase
*protein lmw dsp2
***protein tyrosine phosphatase**
4 nitrophenyl phosphate
vanadate sodium
fluoride sodium
pyrophosphate
okadaic acid
aspartic acid
cysteine
stress activated protein kinase: EC, endogenous compound
mitogen activated protein kinase 1: EC, endogenous compound
mitogen activated protein kinase 2: EC, endogenous compound
unclassified drug

RN (phosphatase) 9013-05-2; (**protein tyrosine phosphatase**) 79747-53-8, 97162-86-2; (**4 nitrophenyl phosphate**) **330-13-2**; (vanadate sodium) 11105-06-9, 13718-26-8, 13721-39-6; (fluoride sodium) 51668-54-3, 7681-49-4, 79933-27-0; (pyrophosphate) 14000-31-8, 7722-88-5, 7758-16-9; (okadaic acid) 78111-17-8; (aspartic acid) 56-84-8, 6899-03-2; (cysteine) 4371-52-2, 52-89-1, 52-90-4; (stress activated protein kinase) 155215-87-5; (mitogen activated protein kinase 1) 137632-07-6; (mitogen activated protein kinase 2) 137632-08-7

GEN GENBANK AF237619 submitted number; GENBANK M32599 referred number; GENBANK U10871 referred number; GENBANK U81823 referred number; GENBANK Y13439 referred number; GENBANK AB005663 referred number; GENBANK AF135185 referred number; GENBANK AB005664 referred number; GENBANK AB005665 referred number

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AN **2003453747** EMBASE

TI Acquisition of a Specific and Potent PTP1B Inhibitor from a Novel Combinatorial Library and Screening Procedure.

AU Shen K.; Keng Y.-F.; Wu L.; Guo X.-L.; Lawrence D.S.; Zhang Z.-Y.

CS D.S. Lawrence, Dept. of Biochemistry, Albert Einstein College of Medicine, Yeshiva University, 1300 Morris Park Ave., Bronx, NY 10461, United States. dlawrenc@aecom.yu.edu

SO Journal of Biological Chemistry, (14 Dec 2001) 276/50 (47311-47319).
Refs: 52
ISSN: 0021-9258 CODEN: JBCHA3
CY United States
DT Journal; Article
FS 029 Clinical Biochemistry
037 Drug Literature Index
LA English
SL English

AB **Protein-tyrosine phosphatases** (PTPases) form a large family of enzymes that serve as key regulatory components in signal transduction pathways. Defective or inappropriate regulation of PTPase activity leads to aberrant tyrosine phosphorylation, which contributes to the development of many human diseases including cancers and diabetes. For example, recent gene knockout studies in mice identify PTP1B as a promising target for anti-diabetes/obesity drug discovery. Thus, there is intense interest in obtaining specific and potent PTPase inhibitors for biological studies and pharmacological development. However, given the highly conserved nature of the PTPase active site, it is unclear whether selectivity in PTPase inhibition can be achieved. We describe a combinatorial approach that is designed to target both the active site and a unique peripheral site in PTP1B. Compounds that can simultaneously associate with both sites are expected to exhibit enhanced affinity and specificity. We also describe a novel affinity-based high-throughput assay procedure that can be used for PTPase inhibitor screening. The combinatorial library/high-throughput screen protocols furnished a small molecule PTP1B inhibitor that is both potent (K(i) = 2.4 nM) and selective (little or no activity against a panel of phosphatases including Yersinia PTPase, SHP1, SHP2, LAR, HePTP, PTP.alpha., CD45, VHR, MKP3, Cdc25A, Stp1, and PP2C). These results demonstrate that it is possible to acquire potent, yet highly selective inhibitors for individual members of the large PTPase family of enzymes.

CT Medical Descriptors:
*enzyme inhibition
*inhibition kinetics
combinatorial library
DNA screening
protein family
regulatory mechanism
signal transduction
enzyme regulation
enzyme phosphorylation
cancer risk
diabetes mellitus
enzyme specificity
drug potency
enzyme active site
binding site
binding affinity
Yersinia
nonhuman
article
priority journal
Drug Descriptors:
***protein tyrosine phosphatase inhibitor: PD, pharmacology**
***protein tyrosine phosphatase 1b inhibitor: PD, pharmacology**
phosphotransferase: EC, endogenous compound
protein shp1: EC, endogenous compound
protein shp2: EC, endogenous compound
protein lar: EC, endogenous compound
protein heptp: EC, endogenous compound
protein tyrosine phosphatase alpha: EC, endogenous compound
CD45 antigen: EC, endogenous compound
protein vhr: EC, endogenous compound
protein Mkp3: EC, endogenous compound
protein tyrosine phosphatase: EC, endogenous compound
protein cdc25a: EC, endogenous compound
protein stp1: EC, endogenous compound
protein pp2c: EC, endogenous compound
unclassified drug
RN (phosphotransferase) 9031-09-8, 9031-44-1; (**protein tyrosine phosphatase**) 79747-53-8, 97162-86-2

AN **2001438829** EMBASE

TI Structure of **protein tyrosine phosphatase** 1B
in complex with inhibitors bearing two phosphotyrosine mimetics.
AU Jia Z.; Ye Q.; Dinaut A.N.; Wang Q.; Waddleton D.; Payette P.;
Ramachandran C.; Kennedy B.; Hum G.; Taylor S.D.
CS S.D. Taylor, Department of Chemistry, University of Waterloo, Waterloo,
Ont. N2L 3G1, Canada. s5taylor@sciborg.uwaterloo.ca
SO Journal of Medicinal Chemistry, (20 Dec 2001) 44/26 (4584-4594).
Refs: 60
ISSN: 0022-2623 CODEN: JMCMAR
CY United States
DT Journal; Article
FS 003 Endocrinology
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB **Protein tyrosine phosphatases** (PTPases) are
signal-transducing enzymes that dephosphorylate intracellular proteins
that have phosphorylated tyrosine residues. It has been demonstrated that
protein tyrosine phosphatase 1B (PTP1B) is an
attractive therapeutic target because of its involvement in regulating
insulin sensitivity (Elcheby et al. Science 1999, 283, 1544-1548). The
identification of a second binding site in PTP1B (Puius et al., Proc.
Natl. Acad. Sci. U.S.A. 1997, 94, 13420-13425) suggests a new strategy for
inhibitor design, where appropriate compounds may be made to
simultaneously occupy both binding sites to gain much higher affinity and
selectivity. To test this hypothesis and gain further insights into the
structural basis of inhibitor binding, we have determined the crystal
structure of PTP1B complexed with two non-peptidyl inhibitors, 4 and 5,
both of which contain two aryl difluoromethylenephosphonic acid groups, a
nonhydrolyzable phosphate mimetic. The structures were determined and
refined to 2.35 and 2.50 A resolution, respectively. Although one of the
inhibitors seems to have satisfied the perceived requirement for dual
binding, it did not bind both the active site and the adjacent
noncatalytic binding site as expected. The second or distal phosphonate
group instead extends into the solvent and makes water-mediated
interactions with Arg-47. The selectivity of the more potent of these two
inhibitors, as well as four other inhibitors bearing two such phosphate
mimetics for PTP1B versus seven other PTPases, was examined. In general,
selectivity was modest to good when compared to PTPases Cdc25a, PTPmeg-1,
PTP.beta., and CD45. However, selectivity was generally poor when compared
to other PTPases such as SHP-1, SHP-2, and especially TCPTP, for which
almost no selectivity was found. The implications these results have
concerning the utility of dual-binding inhibitors are discussed.
CT Medical Descriptors:
signal transduction
drug structure
dephosphorylation
drug targeting
insulin sensitivity
drug binding site
drug selectivity
crystal structure
complex formation
article
Drug Descriptors:
protein tyrosine phosphatase
protein tyrosine phosphatase 1B
protein tyrosine phosphatase inhibitor: AN, drug analysis
protein tyrosine phosphatase inhibitor: DV, drug development
protein tyrosine phosphatase inhibitor: PD, pharmacology
phosphotyrosine
unclassified drug
RN (**protein tyrosine phosphatase**) 79747-53-8,
97162-86-2; (phosphotyrosine) 21820-51-9

L51 ANSWER 4 OF 11 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN **2001176680** EMBASE
TI Phospho-azatyrosine, a less effective **protein-tyrosine**
phosphatase substrate than **phosphotyrosine.**
AU Burke T.R. Jr.; Yao Z.-J.; Ye B.; Miyoshi K.; Otaka A.; Wu L.; Zhang Z.-Y.
CS T.R. Burke Jr., Division of Basic Sciences, National Cancer Institute,
National Institutes of Health, Boyles Street, Frederick, MD 21702-1201,
United States. tburke@helix.nih.gov
SO Bioorganic and Medicinal Chemistry Letters, (21 May 2001) 11/10

(1265-1268).
Refs: 21
ISSN: 0960-894X CODEN: BMCLE8
PUI S 0960-894X(01)00197-4
CY United Kingdom
DT Journal; Article
FS 030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Azatyrosine (AzaTyr, 4) is a natural product isolated from Streptomyces chibanesis, whose structure is characterized by a nitrogen atom in the aryl ring of a tyrosyl residue. This seemingly minor modification to the tyrosyl residue results in profound physiological effects, as AzaTyr has been shown to promote permanent reversion of ras-dependent transformed cells to the normal phenotype in culture and to inhibit chemical induction of carcinogenesis in transgenic mice bearing oncogenic human ras. The mechanisms underlying these effects are not known, however ras-pathways involve an intricate balance between both protein-tyrosine kinases (PTKs) and **protein-tyrosine phosphatases** (PTPs).
The present study was undertaken to examine the general utility of AzaTyr as a structural motif for PTP inhibitor design by examining the phospho-azatyrosine (pAzaTyr)-containing peptide Ac-Asp-Ala-Asp-Glu-pAzaTyr-Leu-amide (8) in a PTP1 enzyme system. Kinetic analysis indicated that 8 binds with a K(m) value of 210 .mu.M and a catalytic turnover rate, k(cat) of 52 s(-1). This represents a greater than 50-fold reduction in binding affinity relative to the parent phosphotyrosine-containing peptide, indicating that the aryl nitrogen adversely affects binding affinity. The much lower PTP affinity of the pAzaTyr-containing peptide reduces the potential utility of the AzaTyr pharmacophore for PTP inhibitor design. These results are discussed from the point of view that incorporation of AzaTyr residues into proteins could result in perturbation of protein-tyrosine phosphorylation/dephosphorylation cascades that control signal transduction processes, including ras-dependent pathways.
CT Medical Descriptors:
drug design
peptide analysis
kinetics
protein binding
catalysis
binding affinity
enzyme binding
drug utilization
pharmacophore
phosphorylation
dephosphorylation
signal transduction
oncogene ras
drug structure
enzyme inhibition
cell culture
article
Drug Descriptors:
***phosphoazatyrosine: AN, drug analysis**
*phosphoazatyrosine: CM, drug comparison
*phosphoazatyrosine: PR, pharmaceutics
*phosphoazatyrosine: PD, pharmacology
***tyrosine derivative: AN, drug analysis**
*tyrosine derivative: CM, drug comparison
*tyrosine derivative: PR, pharmaceutics
*tyrosine derivative: PD, pharmacology
***enzyme inhibitor: AN, drug analysis**
*enzyme inhibitor: CM, drug comparison
*enzyme inhibitor: PR, pharmaceutics
*enzyme inhibitor: PD, pharmacology
*phosphotyrosine: CM, drug comparison
*phosphotyrosine: PD, pharmacology
protein tyrosine phosphatase 1: EC, endogenous compound
protein tyrosine phosphatase: EC, endogenous compound
acetylaspartylalanylaspartylglutamylphosphrylazatyrosineleucine amide: AN, drug analysis
acetylaspartylalanylaspartylglutamylphosphrylazatyrosineleucine amide: DV, drug development
acetylaspartylalanylaspartylglutamylphosphrylazatyrosineleucine amide: PR, pharmaceutics

acetylaspartylalanylaspartylglutamylphosphrylazatyrosineleucine amide: PD, pharmacology
nitrogen
unclassified drug
RN (tyrosine derivative) 42406-77-9; (phosphotyrosine) 21820-51-9; (**protein tyrosine phosphatase**) 79747-53-8, 97162-86-2; (nitrogen) 7727-37-9

L51 ANSWER 5 OF 11 EMBASE on STN
AN **2000362285** EMBASE
TI **Protein tyrosine phosphatases** (PTPS) as drug targets: Inhibitors of PTP-1B for the treatment of diabetes.
AU Hundahl Moller N.P.; Iversen L.F.; Andersen H.S.; McCormack J.G.
CS N.P. Hundahl Moller, Signal Transduction, Target Cell Biology, Novo Alle, DK-2880 Bagsvaerd, Denmark. nphm@novo.dk
SO Current Opinion in Drug Discovery and Development, (2000) 3/5 (527-540). Refs: 115
ISSN: 1367-6733 CODEN: CODDFF
CY United Kingdom
DT Journal; General Review
FS 030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB The phosphorylation of key proteins on tyrosine residues is an important part of many different intracellular signaling cascade mechanisms triggered by hormones and other agents. The deactivation of such signaling processes is catalyzed by proteintyrosine phosphatases (PTPs), and therefore inhibition of these enzymes is being explored in different indications as a means whereby signaling may be prolonged or even initiated in the absence of the triggering agent. In the case of the signaling cascade initiated by the activation of the insulin receptor, an important gene knockout study in mice has identified PTP-1B as a potential target 'for antidiabetes therapy, and has thus made it a 'focus of attention 'for several groups. Recent advances in the structure-based design of potent and selective inhibitors of this enzyme are described, as well as some preliminary data for such inhibitors in animal models which, together with more recently published data from further studies on PTP-1B knockout mice and from antisense studies, illustrate the potential of this approach for the treatment of both Type I and Type II diabetes.
CT Medical Descriptors:
*diabetes mellitus: DT, drug therapy
drug design
drug screening
drug receptor binding
signal transduction
enzyme inhibition
insulin sensitivity
enzyme phosphorylation
protein domain
knockout mouse
glucose homeostasis
human
nonhuman
review
Drug Descriptors:
***protein tyrosine phosphatase: EC, endogenous compound**
***protein tyrosine phosphatase inhibitor: AN, drug analysis**
***protein tyrosine phosphatase inhibitor: DV, drug development**
***protein tyrosine phosphatase inhibitor: DT, drug therapy**
***protein tyrosine phosphatase inhibitor: PD, pharmacology**
glucose
isoenzyme: EC, endogenous compound
protein tyrosine phosphatase 1b: EC, endogenous compound
insulin receptor: EC, endogenous compound
insulin receptor kinase: EC, endogenous compound
CD45 antigen: EC, endogenous compound
acid phosphatase: EC, endogenous compound
antisense oligonucleotide
leptin: EC, endogenous compound
insulin: EC, endogenous compound
triacylglycerol: EC, endogenous compound
naphthalene derivative: AN, drug analysis
naphthalene derivative: DV, drug development
naphthalene derivative: PD, pharmacology

vanadium derivative: AN, drug analysis
vanadium derivative: DT, drug therapy
vanadium derivative: PD, pharmacology
2 (oxalylamino)benzoic acid: AN, drug analysis
2 (oxalylamino)benzoic acid: DV, drug development
2 (oxalylamino)benzoic acid: PD, pharmacology
unclassified drug
RN (**protein tyrosine phosphatase**) 79747-53-8, 97162-86-2; (glucose) 50-99-7, 84778-64-3; (acid phosphatase) 9001-77-8, 9025-88-1; (insulin) 9004-10-8
CO Novo Nordisk; Merck Frosst; Pharmacia Upjohn; Home Products

L51 ANSWER 6 OF 11 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN **2000053341** EMBASE
TI Structure-based discovery of small molecule inhibitors targeted to **protein tyrosine phosphatase** 1B.
AU Sarmiento M.; Wu L.; Keng Y.-F.; Song L.; Luo Z.; Huang Z.; Wu G.-Z.; Yuan A.K.; Zhang Z.-Y.
CS Z.-Y. Zhang, Department of Molecular Pharmacology, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY 10461, United States. zyzhang@aecom.yu.edu
SO Journal of Medicinal Chemistry, (27 Jan 2000) 43/2 (146-155).
Refs: 64
ISSN: 0022-2623 CODEN: JMCMAR
CY United States
DT Journal; Article
FS 029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB **Protein tyrosine phosphatases** (PTPases) are involved in the control of tyrosine phosphorylation levels in the cell and are believed to be crucial for the regulation of a multitude of cellular functions. A detailed understanding of the role played by PTPases in various signaling pathways has not yet been achieved, and potent and selective PTPase inhibitors are essential in the quest to determine the functionality of individual PTPases. Using the DOCK methodology, we have carried out a structure-based, computer- assisted search of an available chemical database in order to identify low molecular weight, nonpeptidic PTP1B inhibitors. We have identified several organic molecules that not only possess inhibitory activity against PTP1B but which also display significant selectivity for PTP1B. This indicates that although structural features important for pTyr recognition are conserved among different PTPases, it is possible to generate selective inhibitors targeted primarily to the catalytic site. Kinetic analysis and molecular modeling experiments suggest that the PTP1B active site possesses significant plasticity such that substituted and extended aromatic systems can be accommodated. The newly identified molecules provide a molecular framework upon which therapeutically useful compounds can ultimately be based, and systematic optimization of these lead compounds is likely to further enhance their potency and selectivity.
CT Medical Descriptors:
*drug targeting
protein phosphorylation
cell function
signal transduction
structure activity relation
molecular interaction
article
Drug Descriptors:
***protein tyrosine phosphatase inhibitor: AN, drug analysis**
***protein tyrosine phosphatase inhibitor: DV, drug development**
***protein tyrosine phosphatase inhibitor: PD, pharmacology**

L51 ANSWER 7 OF 11 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN **2000053013** EMBASE
TI Synthesis and biological evaluation of a targeted library of protein phosphatase inhibitors.
AU Wipf P.; Asian D.C.; Luci D.K.; Southwick E.C.; Lazo J.S.
CS P. Wipf, Department of Chemistry, University of Pittsburgh, Pittsburgh, PA 15260, United States
SO Biotechnology and Bioengineering, (2000) 71/1 (58-70).
Refs: 34

ISSN: 0006-3592 CODEN: BIBIAU
CY United States
DT Journal; Article
FS 030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Phosphorylation of serine, threonine, and tyrosine controls fundamental mammalian cell events and is achieved by kinases which, in turn, are in dynamic relationship with phosphatases. Few selective inhibitors of protein tyrosine and dual specificity phosphatases are readily available. Based on SAR studies of naturally occurring phosphatase inhibitors and following up on previously published research, we have designed a new pharmacophore model V and synthesized a new library of functional analogues of V. All synthetic steps were carried out and optimized employing combinatorial chemistry methods on Wang resin. All compounds were tested in vitro for their ability to inhibit recombinant human protein tyrosine (PTP1B) and dual-specificity (Cdc25B2 and VHR) phosphatases. Three of the approximately 70 compounds in our library inhibited Cdc25B2 by 50% at 375-490 .mu.M. No compounds inhibited PTP1B, and only one blocked VHR. Cell-culture studies revealed no toxicity to human breast cancer cells with two of the phosphatase inhibitors. (C) 2000 John Wiley and Sons, Inc.
CT Medical Descriptors:
*drug synthesis
protein phosphorylation
structure activity relation
in vitro study
pharmacophore
enzyme inhibition
enzyme activity
breast cancer
cell proliferation
human
controlled study
human cell
article
Drug Descriptors:
***phosphoprotein phosphatase inhibitor: AN, drug analysis**
*phosphoprotein phosphatase inhibitor: DV, drug development
*phosphoprotein phosphatase inhibitor: PD, pharmacology
protein tyrosine phosphatase
phosphoprotein phosphatase
resin
cyanoginosin LR
okadaic acid
calyculin A
sulfonamide
amine
amide
lysine derivative
RN (**protein tyrosine phosphatase**) 79747-53-8, 97162-86-2; (phosphoprotein phosphatase) 9025-75-6; (cyanoginosin LR) 101043-37-2; (okadaic acid) 78111-17-8; (calyculin A) 101932-71-2; (amide) 17655-31-1

L51 ANSWER 8 OF 11 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN **1998394517** EMBASE
TI Src Homology-2 Domains: Structure, mechanisms, and drug discovery.
AU Sawyer T.K.
CS T.K. Sawyer, ARIAD Pharmaceuticals, Inc., 26 Landsdowne St., Cambridge, MA 02139, United States. tomi.sawyer@ariad.com
SO Biopolymers - Peptide Science Section, (1998) 47/3 (243-261).
Refs: 44
ISSN: 0006-3525 CODEN: BPSSFT
CY United States
DT Journal; General Review
FS 029 Clinical Biochemistry
037 Drug Literature Index
LA English
SL English
AB Src homology-2 (SH2) domains and their associated catalytic or noncatalytic proteins constitute critical signal transduction targets for drug discovery. Such SH2 proteins are found in the regulation of a number of cellular processes, including growth, mitogenesis, motility,

metabolism, immune response, and gene transcription. From the relationship of tyrosine phosphorylation and intracellular regulation by protein-tyrosine kinases (PTKs) and **protein-tyrosine phosphatases** (PTPs), the dynamic and reversible binding interactions of SH2 domain containing proteins with their cognate phosphotyrosine (pTyr) containing proteins provide a third dimensionality to the orchestration of signal transduction pathways that exist as a result of pTyr formation, degradation, and molecular recognition events. This review highlights several key research achievements impracting our current understanding of SH2 structure, mechanisms, and drug discovery that underlie the role(s) of SH2 domains in signal transduction processes, cellular functions, and disease states.

CT Medical Descriptors:
*protein structure
*sequence homology
***drug screening**
*signal transduction
catalysis
cell growth
mitogenesis
cell motility
cell metabolism
immune response
genetic transcription
protein phosphorylation
protein protein interaction
molecular recognition
drug targeting
drug design
structure activity relation
human
nonhuman
review
Drug Descriptors:
*protein tyrosine kinase: EC, endogenous compound
*protein kinase p60: EC, endogenous compound
***protein tyrosine phosphatase: EC, endogenous compound**
phosphotyrosine: EC, endogenous compound
phosphopeptide
peptide library
protein tyrosine kinase inhibitor: AN, drug analysis
protein tyrosine kinase inhibitor: DV, drug development
protein kinase inhibitor: AN, drug analysis
protein kinase inhibitor: DV, drug development
protein tyrosine phosphatase inhibitor: AN, drug analysis
protein tyrosine phosphatase inhibitor: DV, drug development
nonapeptide: AN, drug analysis
nonapeptide: DV, drug development
prodrug

RN (protein tyrosine kinase) 80449-02-1; (**protein tyrosine phosphatase**) 79747-53-8, 97162-86-2; (phosphotyrosine) 21820-51-9

L51 ANSWER 9 OF 11 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN **1998394516** EMBASE
TI **Protein-tyrosine phosphatases**: Structure, mechanism, and inhibitor discovery.
AU Burke T.R. Jr.; Zhang Z.-Y.
CS T.R. Burke Jr., Building 37, National Institutes of Health, Bethesda, MD 20892, United States
SO Biopolymers - Peptide Science Section, (1998) 47/3 (225-241).
Refs: 190
ISSN: 0006-3525 CODEN: BPSSFT
CY United States
DT Journal; General Review
FS 029 Clinical Biochemistry
037 Drug Literature Index
LA English
SL English
AB Protein-tyrosine kinases (PTKs) and their associated signaling pathways are crucial for the regulation of numerous cell functions including growth, mitogenesis, motility, cell-cell interactions, metabolism, gene transcription, and the immune response. Since tyrosine phosphorylation is reversible and dynamic in vivo, the phosphorylation states of proteins are governed by the opposing actions of PTKs and **protein-tyrosine phosphatases** (PTPs). In this light, both PTKs

and PTPs play equally important roles in signal transduction in eukaryotic cells, and comprehension of mechanisms behind the reversible pTyr-dependent modulation of protein function and cell physiology must necessarily encompass the characterization of PTPs as well as PTKs. In spite of the large number of PTPs identified to date and the emerging role played by PTPs in disease, a detailed understanding of the role played by PTPs in signaling pathways has been hampered by the absence of PTP-specific agents. Such PTP-specific inhibitors could potentially serve as useful tools in determining the physiological significance of protein tyrosine phosphorylation in complex cellular signal transduction pathways and may constitute valuable therapeutics in the treatment of several human diseases. The goal of this review is therefore to summarize currently understandings of PTP structure and mechanism of catalysis and the relationship of these to PTP inhibitor development. The review is organized such that enzyme structure is covered first, followed by mechanisms of catalysis then PTP inhibitor development. In discussing PTP inhibitor development, nonspecific inhibitors and those obtained by screening methods are initially presented with the focus then shifting to inhibitors that utilize a more structure-based rationale.

CT Medical Descriptors:
*enzyme structure
*enzyme mechanism
***protein phosphorylation**
***drug screening**
signal transduction
catalysis
cell growth
mitogenesis
cell motility
cell interaction
cell metabolism
genetic transcription
immune response
osteoclast
human
nonhuman
review
Drug Descriptors:
***protein tyrosine phosphatase: EC, endogenous compound**
***protein tyrosine phosphatase inhibitor: DV, drug development**
natural product
apomorphine
acid phosphatase prostate isoenzyme
alkaline phosphatase bone isoenzyme
phosphonic acid derivative: DV, drug development
alendronic acid: DV, drug development
peptide library

RN (**protein tyrosine phosphatase**) 79747-53-8, 97162-86-2; (apomorphine) 314-19-2, 58-00-4; (alendronic acid) 66376-36-1

L51 ANSWER 10 OF 11 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN **97331069** EMBASE
DN 1997331069
TI A combinatorial approach to identifying **protein tyrosine phosphatase** substrates from a phosphotyrosine peptide library.
AU Cheung Y.W.; Abell C.; Balasubramanian S.
CS S. Balasubramanian, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, United Kingdom
SO Journal of the American Chemical Society, (1997) 119/40 (9568-9569).
Refs: 25
ISSN: 0002-7863 CODEN: JACSAT
CY United States
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
CT Medical Descriptors:
*enzyme specificity
***protein phosphorylation**
article
methodology
screening
sequence analysis
Drug Descriptors:
*phosphotyrosine
***protein tyrosine phosphatase**

RN (phosphotyrosine) 21820-51-9; (**protein tyrosine phosphatase**) 79747-53-8, 97162-86-2

L51 ANSWER 11 OF 11 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN **95359852** EMBASE
DN 1995359852
TI Synthetic Tyr-phospho and non-hydrolyzable phosphonopeptides as PTKs and TC-PTP inhibitors.
AU Ruzza P.; Deana A.D.; Calderan A.; Pavanetto M.; Cesaro L.; Pinna L.A.; Borin G.
CS Centro di Studio sui Biopolimeri, CNR, Dipart. di Chimica Organica, Universita di Padova, Via Marzolo 1,35131 Padova, Italy
SO International Journal of Peptide and Protein Research, (1995) 46/6 (535-546).
ISSN: 0367-8377 CODEN: IJPPC3
CY Denmark
DT Journal; Article
FS 029 Clinical Biochemistry
037 Drug Literature Index
LA English
SL English
AB **Tyrosine**-specific **protein** kinases and **phosphatases** are important signal transducing enzymes in normal cellular growth and differentiation and have been implicated in the etiology of a number of human neoplastic processes. In order to develop agents which inhibit the function of these two classes of enzymes by interfering with the binding of their substrates, we synthesized analogs derived from the peptide EDNEYTA. This sequence reproduces the main autophosphorylation site of Src tyrosine kinases. In this work we report the synthesis, by classical solution methods, of the phosphotyrosyl peptide EDNEYpTA as well as of three analogs in which the phosphotyrosine is replaced by a phosphinotyrosine and by two unnatural, non-hydrolyzable amino acids 4-phosphonomethyl-L-phenylalanine and 4-phosphono-L-phenylalanine. The Src peptide and its derivatives were tested as inhibitors of three non-receptor tyrosine kinases (Lyn, belonging to the Src family, CSK and PTK-IIB) and a non-receptor **protein tyrosine phosphatase** obtained from human T-cell (TC-PTP). The biomimetic analogues, which do not significantly affect the activity of CSK, PTK-IIB and TC-PTP, act as efficient inhibitors on Lyn, influencing both the exogenous phosphorylation and, especially, its autophosphorylation. In particular, the Pphe derivative may provide a basis for the design of a class of inhibitors specific for Lyn and possibly Src tyrosine kinases, capable of being used in vivo and in vitro conditions.
CT Medical Descriptors:
*enzyme inhibition
article
autophosphorylation
circular dichroism
controlled study
drug design
human
human cell
peptide synthesis
protein phosphorylation
protein structure
structure activity relation
t lymphocyte
Drug Descriptors:
***enzyme inhibitor: AN, drug analysis**
*enzyme inhibitor: CM, drug comparison
*enzyme inhibitor: DV, drug development
*protein tyrosine kinase: PR, pharmaceutics
***protein tyrosine phosphatase: EC, endogenous compound**
***synthetic peptide: AN, drug analysis**
*synthetic peptide: CM, drug comparison
*synthetic peptide: DV, drug development
RN (protein tyrosine kinase) 80449-02-1; (**protein tyrosine phosphatase**) 79747-53-8, 97162-86-2

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L60 ANSWER 1 OF 3 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
AN **2001-235905** [25] WPIX
DNC C2001-070998
TI Identifying a combination of a **dephosphorylating** enzyme and a phosphorylated protein that forms a complex involved in the control of cell regulation comprises oxidatively deactivating the enzyme.
DC B04 D16
IN BOEHMER, F; HERRLICH, P
PA (GESL) FORSCHUNGSZENTRUM KARLSRUHE GMBH
CYC 20
PI DE 10035472 A1 20010315 (200125)* 25 C12N009-14
WO 2001020021 A2 20010322 (200125) GE C12Q001-42
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: JP US
ADT DE 10035472 A1 DE 2000-10035472 20000721; WO 2001020021 A2 WO 2000-EP7455 20000802
PRAI DE 1999-19944069 19990914
IC ICM C12N009-14; C12Q001-42
ICS A61K038-17; A61K038-45; A61K038-46; C07K014-435; C07K014-71; C12N009-12; C12N009-16; C12N013-00; C12Q001-48; G01N033-68
AB DE 10035472 A UPAB: 20010508
NOVELTY - Method (M) for identifying a combination of a **dephosphorylating** enzyme and a phosphorylated protein that forms a complex involved in the control of cell regulation, in new
DETAILED DESCRIPTION - Method (M) for identifying a combination of a **dephosphorylating** enzyme and a phosphorylated protein that forms a complex involved in the control of cell regulation comprises:
(a) providing a system comprising at least one **dephosphorylating** enzyme and at least one phosphorylated protein;
(b) deactivating the enzyme(s) by oxidation;
(c) isolating any complex not undergoing catalytic conversion; and
(d) identifying the components of the complex.
INDEPENDENT CLAIMS are also included for the following:
(1) a complex (I) comprising an oxidatively deactivated **dephosphorylating** enzyme and a phosphorylated protein;
(2) the **dephosphorylating** enzyme (II) contained in (I);
(3) the phosphorylated protein (III) contained in (I);
(4) a substrate of (III) that forms a complex with (II);
(5) a method (M1) for deactivating a **dephosphorylating** enzyme, comprising exposing the enzyme, or cells containing it, to radiation, oxidizing agents and/or alkylating agents;
(6) **dephosphorylated** (sic) enzymes produced by (M1);
(7) a screening (M2) assay for effectors of (I), (II) or (III), comprising:
(a) either incubating (I), (II) or (III) with at least one test substance or irradiating (I), (II) or (III);
(b) measuring the specific activity of (II) and/or degree of phosphorylation of (III);
(c) repeating step (b) in the absence of the test substance(s) or without irradiation; and
(d) comparing the results from steps (b) and (c);

(8) effectors identified by (M2).

USE - Enzyme-protein (especially phosphatase-kinase) pairs identified by the method are useful as targets in screening assays and drug development programs aimed at finding agents capable of modulating the control mechanisms of cell regulation, signal transduction, cell proliferation and/or cell differentiation, especially agents for treating neurodegenerative diseases, diabetes, atherosclerosis or cancer.

Dwg.0/12

FS CPI

FA AB; DCN

MC CPI: B04-K01; B04-L04; B04-L05; **B11-C08E**; B11-C09; B12-K04E; D05-H09

TECH UPTX: 20010508

TECHNOLOGY FOCUS - BIOLOGY - Preferred Method: The enzyme is a **protein tyrosine phosphatase** and the **protein** is a protein tyrosine kinase, especially a cell surface receptor with tyrosine kinase activity.

The system of step (a), of the method (M), is an artificial system or a natural system, preferably a living cell, especially a mammalian cell. The enzyme is reversibly deactivated so that it binds to the protein without catalytically converting it, preferably by oxidizing an amino acid at its catalytic activity center, either by exposure to radiation, especially ultraviolet radiation with a wavelength of 335, 312 or 200-280 nm, or by treatment with an oxidizing agent, especially hydrogen peroxide, or an alkylating agent.

L60 ANSWER 2 OF 3 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN

AN **1999-327025** [27] WPIX

DNN N1999-245288 DNC C1999-096772

TI Identifying modulators agents that modulate leptin activity.

DC B04 D16 S03

IN FRIEDMAN, J M; LI, C

PA (UYRQ) UNIV ROCKEFELLER

CYC 21

PI WO 9923493 A1 19990514 (199927)* EN 86 G01N033-68

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: CA JP MX

ADT WO 9923493 A1 WO 1998-US22797 19981027

PRAI US 1998-178691 19981026; US 1997-961809 19971031

IC ICM G01N033-68

ICS G01N033-573; G01N033-74

AB WO 9923493 A UPAB: 19990714

NOVELTY - A method for identifying agents that modulate leptin activity, is new.

DETAILED DESCRIPTION - The method of identifying a modulator of binding of a phosphorylated leptin receptor with tyrosine phosphatase 1D (PTP-1D) comprises:

(a) contacting a tyrosine-985 phosphorylated leptin receptor or its phosphorylated fragment with **protein tyrosine phosphatase** 1D (PTP-1D) or its fragment in the presence and absence of a candidate agent under conditions in which in the absence of the agent the binding of the phosphorylated leptin receptor or fragment with PTP-1D or its fragment can be detected; and

(b) detecting the binding of the phosphorylated leptin receptor and PTP 1d;

where an increase in binding detected in the presence of the agent, indicates that the agent enhances binding, and a decrease in binding in the presence of the agent indicates that the agent is a binding inhibitor.

INDEPENDENT CLAIMS are also included for the following:

(1) identifying modulators of phosphorylated leptin receptor-dependent PTP-1D phosphorylation, optionally in situ;

(2) identifying modulators of leptin-dependent PTP-1D **dephosphorylation** of JAK2 kinase in situ;

(3) identifying inhibitors of leptin-dependent PTP-1D phosphorylation in situ; and

(4) identifying drugs useful in a weight loss diet regimen.

ACTIVITY - Anorectic.

MECHANISM OF ACTION - Enzyme Inhibitor.

USE - Modulators of tyrosine-985-phosphorylated leptin receptor-dependent PTP-1D phosphorylation are useful as drugs in weight loss diet regimens. The drugs identified can regulate adiposity and fat content of animals, particularly in mammals. Disorders that can be treated by PTP-1D modulators include obesity and its associated diseases, e.g. hypertension, heart disease and type II diabetes, and weight loss associated with cancer and AIDS. Additionally the agents identified may be useful in agriculture where body weight of domestic animals can be

modulated.
FS CPI EPI
FA AB; DCN
MC CPI: B04-K01; **B11-C08**; B12-K04A; D05-H09; D05-H10
EPI: S03-E14H; S03-E14H4
TECH UPTX: 19990714
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Methods: The phosphorylated leptin receptor or its phosphorylated fragment is bound to a solid support. The phosphorylated fragment is part of a fusion protein, i.e. fused to glutathione-S-transferase or green fluorescent protein. PTP-1D or its fragment is labeled.
Modulators of tyrosine-985 phosphorylated leptin receptor dependent PTP-1D phosphorylation can be identified by contacting the receptor with PTP-1D and JAK2 kinase in the presence and absence of an agent. Absence of the agent allows phosphorylation of PTP-1D. The amount of PTP-1D phosphorylation is measured in the presence and absence of the agent. Potential modulators are then contacted with PTP-1D and JAK2 in the absence of a phosphorylated receptor. When no significant change in phosphorylation is determined in the presence of the potential modulator relative to that in the absence of the potential modulator, the potential modulator is a modulator of the leptin-dependent phosphorylation of PTP-1D.
The method of (2) comprises contacting a cell with leptin in the presence or absence of an agent under conditions in which in the absence of the agent leptin induces the phosphorylation of PTP-1D, where the cell comprises PTP-1D, JAK2, and a tyrosine-985 leptin receptor. The amount of PTP-1D phosphorylation is then measured, where an increase or decrease in phosphorylation of PTP-1D is determined in the presence of the agent relative to in the absence of the agent. This method uses cells transfected with vectors encoding PTP-1D, JAK2 and a leptin receptor containing tyrosine-985. The method of (2) further comprises contacting a second cell with leptin and the potential modulator under the conditions described above except where the leptin cannot induce phosphorylation of PTP-1D and where the second cell is transfected with vectors encoding PTP-1D, JAK2 and a leptin receptor that does not contain a tyrosine-985. A modulator is identified when there is no significant change in phosphorylation in the presence of the potential modulator relative to in the absence of the potential modulator. The leptin receptor that does not contain tyrosine-985 is Ob-Ra or Ob-Rb containing a phenylalanine-985. The modulator can enhance or inhibit the leptin receptor-dependent phosphorylation of PTP-1D.
An inhibitor of leptin-dependent PTP-1D phosphorylation can be identified in a similar manner, where in the absence of the agent, leptin induces the expression of a reporter gene operably under the control of a promoter containing a binding site for activated Stat3. Modulators of leptin-dependent PTP-1D **dephosphorylation** of JAK2 kinase can also be identified in situ in a similar manner.
The modulators identified can be administered to test animals. Modulators that causes the test animal to lose weight relative to a control animal (receiving multiple doses of a placebo) are selected as a drug useful in weight loss diet regimens.

L60 ANSWER 3 OF 3 WPIX COPYRIGHT 2004 THE THOMSON CORP on STN
AN **1997-424288** [39] WPIX
DNC C1997-135768
TI **Protein tyrosine phosphatase** src homology domain binding peptide - corresponds to the phosphatase binding site in EPO receptor, used to prolong the effect of EPO and to identify other phosphatase(s).
DC B04 D16
IN KLINGMUELLER, U; LODISH, H F; MICHNICK, S
PA (WHED) WHITEHEAD INST BIOMEDICAL RES
CYC 1
PI US 5659012 A 19970819 (199739)* 14 A61K038-04
ADT US 5659012 A US 1995-402006 19950310
PRAI US 1995-402006 19950310
IC ICM A61K038-04
AB US 5659012 A UPAB: 19990525
A peptide (A) which binds to the src homology-2 domain of **protein tyrosine phosphatase** (PTP) SH-PTP1 is new. TPPHLKYLYVVS
(A) Also claimed are derivatives of (A) having at least one amino acid modified by substitution with a fluoroether, methyl ether or thioether group.
USE - (A) represents the site in erythropoietin receptor (EPO-R) to which SH-PTP1 binds, resulting in activation of phosphatase activity, **dephosphorylation** of the receptor and of JAK2 kinase, so that the

EPO proliferative signal is ended. (A) can be used as an affinity reagent to identify other phosphatases that bind to EPO-R, also therapeutically to prolong the effect of EPO, e.g. where this is being used to stimulate haemoglobin synthesis or to treat anaemia (associated with renal failure, chronic disease, HIV infection, blood loss or cancer).
Dwg.0/4
FS CPI
FA AB; DCN
MC CPI: B04-C01C; **B11-C08E3**; B12-K04; B14-H01; D05-H17A4

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